Ⅴ．研究成果の刊行に関する一覧表

雑誌

発表者氏名	論文タイトル名	発表誌名	巻号	ページ	出版年
東福寺幾夫、澤井高志	バーチャルスライドの利用と標準化に関する調査報告	日本遠隔医療学会雑誌	8	19－24	2012
中山育徳、松村翼、赤坂俊英、澤井高志	皮膚科領域における virtual slide を利用した遠隔病理診断用コンサルテーションシステムの開発	岩手医誌	64	173－182	2012
Nakai K, Itoh M, Okabayashi H, Tsuboi J, Mitsunaga Y, Komatsu T, Yoshika K	Body surface Two-dimensional spectral map of atrial fibrillation using vector-projected 187 channel electrocardiography.	Int Heart J	53	5 - 10	2012
Futagawa K, Shoda M, Nakai K, Hiroshi Kasanuki H, Hagiwara N	Spatial distribution of ventricular late potentials assessed by the newly developed signal-averaged vector-projected 187-channel electrocardiogram in patients with old myocardial infarction.	J Arrhythmia	29	28 - 33	2012
小山耕太郎	修正大血管転位症の診断	日小循誌	28	73-80	2012
小山耕太郎	手術を受けた先天性心疾患に対する心エコー：Fallot四徴症修復術後	心エコー	13	296-303	2012
小山耕太郎	東日本大震災・津波と岩手県の医療情報連携・遠隔医療	Rad Fan	10	24-26	2012
高木基宏、藤井寛、小山耕太郎、大平隆、柿沼博一、藤野雄一、澤井高志、猪飼秋夫	遠隔画像診断のためのSVC符号化された心臓超音波画像の主観画像評価	信学技報	111	239-244	2012
Ikai A, Koizumi J, Kin H, Mukaida M, Takahashi S, Oyama K, Okabayashi H	Aortic translocation using the hemi-Mustard procedure for corrected transposition.	Ann Thorac Surg.	94	996-998	2012
江原茂	遠隔画像診断ガイドラインの目指す画像診断のあり方	Japanese J of Clinical Radiology	57	1141-1144	2012
Nakayama I,Matsumura T,Kamataki A, Uzuki M, Saito K, Hobbs J, Akasaka T, Sawai T	Development of a teledermatopathology consultation system using virtual slides.	Diagnostic Pathology	7	177 - 184	2012
Sawai T, Uzuki M, Miura Y, Kamataki A, Matsumura T, Saito K, Kurose A, Osamura Y.R, Yoshimi N, Kanno H, Moriya T, Ishida Y, Satoh Y, Nakao M, Ogawa E, Matsuo S, Kasai H, Kumagai K, Motoda T, Hopson N	World's first telepathology experiments employing WINDS ultra-high-speed internet satellite, nicknamed "KIZUNA"	J Pathol Inform	4	24	2013

Park S, Parwani A, Aller R.D, Banach L, J. Becich M.J, Borkenfel S, Carter A.B, Friedman B.A, Rojo M.G, Georgiou A, Kayser G, Kayser K, Legg M, Naugler C, Sawai T, Weiner H, Winsten D, Pantanowitz L	The history of pathology informatics: a global perspective	Journal of Pathology Informatics	4	7	2013
菅井 有, 澤井 高志	岩手県における遠隔病理診断の現状と今後の展望	日本遠隔医療学会雑誌	9 (1)	10 - 11	2013
赤坂 俊英, 高橋 和宏	三陸沿岸部被災地域との皮膚科遠隔診療の試み	日本遠隔医療学会雑誌	9 (1)	4 - 5	2013
Watanabe A, Yasuhira S, Inoue T, Kasai S, Shibazaki M, Takahashi K, Akasaka T, Masuda T, Maesawa C	BCL2 and BCLxL are key determinants of resistance to antitubulin chemotherapeutics in melanoma cells.	Exp Dermatol	22	518 - 523	2013
Watabe D, Akasaka T	Annular elastolytic giant cell granuloma developing on lesions of vitiligo	Int J of Dermatology	52 (11)	1458 - 1460	2013
Miura S, Shibazaki M, Kasai S, Yasuhira S, Watanabe A, Inoue T, Kageshita Y, Tsunoda K, Takahashi K, Akasaka T, Masuda T, Maesawa C	A somatic mutation of the KEAP1 gene in malignant melanoma is involved in aberrant NRF2 activation and an increase in intrinsic drug resistance	J Invest Dermatol	134	553 - 556	2013
Sakurai E, Satoh T, Yashima-Abo A, Maesawa C, Tsunoda K, Endo M, Akasaka T, Masuda T	Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) with Hemophagocytosis (HPS) : successful treatment using high-dose chemotherapy (BFM-NHL & ALL-90) and autologous peripheral blood stem cell transplantation	J Clinical and Experimental Hematopathology	53 (2)	135 - 140	2013
Tsunoda K, Takahashi K, Maeda F, Oikawa H, Akasaka T	A case of atypical fibrous histocytoma with positivity for CD163 and CD44	Acta Derm Venereol.	93(6)	737 - 738	2013
小川 彰	いわて新医療モデルと遠隔医療	日本遠隔医療学会雑誌	9 (1)	2-3	2013
高橋 義彦	岩手医科大学と県立宮古病院の間の糖尿病遠隔診療支援	日本遠隔医療学会雑誌	9 (1)	8-9	2013
江原 茂	遠隔画像診断を発展させた岩手県広域ネットワークによる画像情報連携にむけて	日本遠隔医療学会雑誌	9 (1)	8-9	2013

Okamoto K, Fujimori T, Yamaguchi T, Ichikawa K, Tomita S, Sugai T, Imura J, Ohkura Y, Yao T, Fujii S, Kusaka T, Sekikawa A, Fukui H, Chiba T, Kato H, Mitomi H	Overexpression of regenerating gene I α appears to reflect aberration of crypt cell compartmentalization in sessile serrated adenoma/polyps of the colon.	Diagn Pathol.	8(1)	187	2013
Mitomo S, Takahara T, Nitta H, Fujita T, Ito N, Uesugi N, Sugai T, Wakabayashi G	Sunitinib treatment enabling resection of massive liver metastasis: a case report.	J Med Case Rep.	7 (1)	234	2013
Yamashita M, Mouri T, Niisato M, Kowada K, Kobayashi H, Chiba R, Satoh T, Sugai T, Sawai T, Takahashi T, Yamauchi K	Heterogeneous characteristics of lymphatic microvasculatures associated with pulmonary sarcoid granulomas.	Ann Am Thorac Soc.	10(2)	90 - 97	2013
Ichikawa K, Fujimori T, Moriya T, Ochiai A, Yoshinaga S, Kushima R, Nagahama R, Ohkura Y, Tanaka S, Ajioka Y, Hirata I, Tanaka M, Hoshihara Y, Kinoshita Y, Sasano H, Iwashita A, Tomita S, Hirota S, Yao T, Fujii S, Matsuda T, Ueno H, Ishikawa Y, Takubo K, Fukushima N, Sugai T, Iwafuchi M, Imura J, Manabe T, Fukayama M	Digestive disease management in Japan: a report on the 6th diagnostic pathology summer fest in 2012.	Digestion	88(3)	153 - 160	2013
Suzuki R, Yamamoto E, Nojima M, Maruyama R, Yamano HO, Yoshikawa K, Kimura T, Harada T, Ashida M, Niinuma T, Sato A, Nosho K, Yamamoto H, Kai M, Sugai T, Imai K, Suzuki H, Shinomura Y	Aberrant methylation of microRNA-34b/c is a predictive marker of metachronous gastric cancer risk.	J Gastroenterol.		13-Aug	2013
Beppu T, Terasaki K, Sasaki T, Fujiwara S, Matsuura H, Ogasawara K, Sera K, Yamada N, Uesugi N, Sugai T, Kudo K, Sasaki M, Ehara S, Iwata R, Takai Y	Standardized Uptake Value in High Uptake Area on Positron Emission Tomography with 18F-FRP170 as a Hypoxic Cell Tracer Correlates with Intratumoral Oxygen Pressure in Glioblastoma.	Mol Imaging Biol.	16 (1)	127 - 135	2013
Kato Y, Konari S, Obara W, Sugai T, Fujioka T	Concurrence of villous adenoma and non-muscle invasive bladder cancer arising in the bladder: a case report and review of the literature.	BMC Urol.	13	36	2013
Kawasaki T, Bussolati G, Castellano I, Marchi? C, Daniele L, Molinaro L, Kondo T, Katoh R, Inoue S, Fujii H, Sugai T, Sapino A	Small-cell carcinoma of the breast with squamous differentiation.	Histopathology	63 (5)	739 - 741	2013
Okamoto Y, Fujimori T, Ohkura Y, Sugai T, Arai T, Watanabe G, Wada R, Ueno H, Togashi K, Yao T, Kushima R, Mitomi H, Tomita S, Igarashi Y, Ichikawa K	Histological assessment of intra- and inter-institutional reliabilities in detection of desmoplastic reaction in biopsy specimens of early colorectal carcinomas.	Pathol Int.	63 (11)	539 - 545	2013
菅井 有，澤井 高志	岩手県における遠隔病理診断の現状と今後の展望	日本遠隔医療学会雑誌	9 (1)	10 - 11	2013

小飯塚仁彦, 菅井 有	【胃癌発生と腸上皮化生】腺管分離法を用いた腸上皮化生腺管、非腸上皮化生腺管、胃癌腺管における癌関連遺伝子のDNAメチル化解析	消化器内科	57(1)	40 - 48	2013
須藤隆之, 藤田倫寛, 御供真吾, 梅邑 晃, 石田 馨, 上杉憲幸, 菅井 有	腺管絨毛腺腫, 高分化腺癌, 内分泌細胞癌が共存した直腸内分泌細胞癌長期生存の1例	日本消化器外科学会雑誌	46(2)	143 - 150	2013
山田範幸, 菅井 有	知っておきたい特殊染色-染色のコツと鏡検のポイント 3. グリメリウス染色.	Medical Technology	41(5)	539 - 544	2013
山田範幸, 菅井 有	5-2 膠原線維染色.	基礎病理技術学		37 - 44	2013
菅井 有, 幅野 渉	【消化管疾患のtrends & topics 2013】分子生物学からみた大腸腺腫の診断と治療(解説/特集)	Mebio	30(6)	84 - 94	2013
上杉憲幸, 菅井 有, 織笠俊輔, 杉本 亮, 遠藤昌樹, 鈴木一幸	微小胃癌の病理 分化型微小胃癌の臨床病理学的および分子病理学的特徴	胃と腸	48(6)	794 - 808	2013
田中義人, 山野泰穂, 吉川 健二郎, 高木 亮, 原田英嗣, 中岡宙子, 青木敬則, 檜森亮吾, 片野優子, 永塚 真, 佐藤健太郎, 今井靖, 菅井 有, 山本英一郎, 鈴木拓	【非腫瘍性大腸ポリープのすべて】主題関連研究 右側結腸における過形成性ポリープからみたSSA/Pとの関連性に関する検討	胃と腸	48(8)	1184 - 1190	2013
菅井 有	【非腫瘍性大腸ポリープのすべて】大腸ポリープ雑考	胃と腸	48(8)	1099 - 1102	2013
菅井 有, 上杉憲幸, 杉本 亮	【非腫瘍性大腸ポリープのすべて】inflammatory myoglandular polypと若年性ポリープの病理学的鑑別 inflammatory myoglandular polypの臨床病理学的特徴	胃と腸	48(8)	1161 - 1174	2013
遠藤昌樹, 藤野靖久, 上杉憲幸, 菅井 有	【非腫瘍性大腸ポリープのすべて】グラフ inflammatory myoglandular polyp	胃と腸	48(8)	1200 - 1201	2013
織笠俊輔, 菅井 有, 松井雄介, 杉本 亮, 遠藤昌樹, 千葉俊美	腫瘍グレードに基づいた分化型早期胃癌の分子病理学的解析	岩手医誌	65(3)	155 - 164	2013
杉本 亮, 織笠俊輔, 松井雄介, 肥田圭介, 若林 剛, 菅井 有	胃癌分離腺管および周囲粘膜における分離腸上皮化生腺管、分離非腸上皮化生腺管の分子病理学的解析	岩手医誌	65(4)	271 - 283	2013
Terata M, Nakai K, Fukushima A, Itoh M, Kikuchi A, Sugiyama T	Detection of Peripartum Myocardial Burden by Vector-Projected 187 Channel Electrocardiography and Serum NT-proBNP.	Int Heart J	54	140 - 145	2013

Oyama R, Jakab M, Kikuchi A, Sugiyama T, Kikinis R, Pujol S	Towards improved ultrasound-based analysis and 3D visualization of the fetal brain using the 3D Slicer.	Ultrasound Obstet Gynecol	42	609 - 610	2013
Kaido Y, Kikuchi A, Kanasugi T, Fukushima A, Sugiyama T	Acute abdomen due to ovarian congestion: a fallopian tube accompanied by a paratubal cyst, coiling tightly round the ovary.	J Obstet Gynaecol Res	39	402 - 405	2013
Kanasugi T, Kikuchi A, Matsumoto A, Terata M, Isurugi C, Oyama R, Fukushima A, Sugiyama T	Monochorionic twin fetus with VACTERL association after intracytoplasmic sperm injection.	Congenital Anomalies	53	95 - 97	2013
Kanasugi T, Kikuchi A, Omi H, Ikeda M, Fukushima A, Sugiyama T	Appendiceal mucocele and peritoneal inclusion cyst mimicking right adnexal masses: a diagnostic challenge in gynecologic practice.	J Med Ultrasonics	40	51 - 55	2013
Terata M, Kikuchi A, Kanasugi T, Oyama R, Fukushima A, Sugiyama T	Prenatal diagnosis of parasitic conjoined twins with three-dimensional ultrasound.	Congenital Anomalies	53	131 - 133	2013
Kaido Y, Kikuchi A, Oyama R, Kanasugi T, Fukushima A, Sugiyama T	Prenatal ultrasound and magnetic resonance imaging findings of a hypovascular epignathus with a favorable prognosis.	J Med Ultrasonics	40	61 - 64	2013
Nakai T, Mano H, Ikeya Y, Sonoda K, Ashino S, Okumura Y, Ohkubo K, Kunimoto S, Kasamaki Y, Watanabe I, Hirayama A, Nakai K	Electrical storm after cardiac resynchronization therapy in a patient with nonischemic cardiomyopathy: Signal-averaged vector-projected 187-channel electrocardiogram-based risk stratification for lethal arrhythmia	J. Arrhythmia	29	353 - 356	2013
Torii S, Ohta H, Morino Y, Nakashima M, Suzuki Y, Murata S, Sakuma Y, Ikari Y, Tamura T	Successful endovascular treatment of rupture of mycotic left main coronary artery aneurysm.	The Canadian journal of cardiology.	29	1014 e7 - 9	2013
Nozue T, Yamamoto S, Tohyama S, Fukui K, Umezawa S, Onishi Y, Kunishima T, Sato A, Nozato T, Miyake S, Takeyama Y, Morino Y, Yamauchi T, Muramatsu T, Hirano T, Hibi K, Terashima M, Michishita I	Impacts of age on coronary atherosclerosis and vascular response to statin therapy.	Heart and vessels.	June		2013
Nozue T, Yamamoto S, Tohyama S, Fukui K, Umezawa S, Onishi Y, Kunishima T, Sato A, Nozato T, Miyake S, Takeyama Y, Morino Y, Yamauchi T, Muramatsu T, Hibi K, Terashima M, Michishita I, Investigators T	Comparison of change in coronary atherosclerosis in patients with stable versus unstable angina pectoris receiving statin therapy (from the Treatment With Statin on Atheroma Regression Evaluated by Intravascular Ultrasound With Virtual Histology [TRUTH] study).	The American journal of cardiology	111	923 - 929	2013

Nozue T, Yamamoto S, Tohyama S, Fukui K, Umezawa S, Onishi Y, Kunishima T, Sato A, Nozato T, Miyake S, Takeyama Y, Morino Y, Yamauchi T, Muramatsu T, Hibi K, Michishita I	Effects of statins on serum n-3 to n-6 polyunsaturated fatty acid ratios in patients with coronary artery disease.	Journal of cardiovascular pharmacology and therapeutics.	18	320 - 326	2013
Nozue T, Fukui K, Yamamoto S, Kunishima T, Umezawa S, Onishi Y, Tohyama S, Takeyama Y, Morino Y, Yamauchi T, Hibi K, Sozu T, Terashima M, Michishita I, Investigators T	C-reactive protein and future cardiovascular events in statin-treated patients with angina pectoris: the extended TRUTH study.	Journal of atherosclerosis and thrombosis.	20	717 725	2013
Natsuaki M, Kozuma K, Morimoto T, Kadota K, Muramatsu T, Nakagawa Y, Akasaka T, Igarashi K, Tanabe K, Morino Y, Ishikawa T, Nishikawa H, Awata M, Abe M, Okada H, Takatsu Y, Ogata N, Kimura K, Urasawa K, Tarutani Y, Shiode N, Kimura T, Investigators N	Biodegradable polymer biolimus-eluting stent versus durable polymer everolimus-eluting stent: a randomized, controlled, noninferiority trial.	Journal of the American College of Cardiology.	62	181 - 190	2013
Kozuma K, Kimura T, Kadota K, Suwa S, Kimura K, Iwabuchi M, Kawai K, Miyazawa A, Kawamura M, Nakao K, Asano R, Yamamoto T, Suzuki N, Aoki J, Kyono H, Nakazawa G, Tanabe K, Morino Y, Igarashi K	Angiographic findings of everolimus-eluting as compared to sirolimus-eluting stents: angiographic sub-study from the Randomized Evaluation of Sirolimus-eluting versus Everolimus-eluting stent Trial (RESET).	Cardiovascular intervention and therapeutics.	28	344 - 351	2013
Komatsu T, Sato Y, Ozawa M, Kunugita F, Ueda H, Tachibana H, Morino Y, Nakamura M	Relationship between CHADS2 score and efficacy of antiarrhythmic drug therapy in patients with paroxysmal atrial fibrillation.	Circulation journal : official journal of the Japanese Circulation Society.	77	639 - 645	2013
Koeda Y, Itoh T, Fusazaki T, Nakamura M, Morino Y	A unique stenosis in saphenous vein graft visualized by optical coherence tomography.	Heart and vessels.	29 (2)	278 - 281	2013
鎌田弘之、車谷浩一、長谷川高志	スマートフォンを用いた新しい心電図伝送システムとホルター心電図法との比較	日本遠隔医療学会雑誌	9 (1)	21 - 23	2013
小山耕太郎	モバイルネットワーク環境における新生児心臓病の超音波動画像遠隔診断	日本遠隔医療学会雑誌	9 (1)	12-14	2013
鳥谷 由貴子, 小山 耕太郎, 松本 敦, 那須 友里恵, 中野 智, 小西 雄, 外舘 玄一朗, 葛西 健郎, 千田 勝一	低出生体重児における臓器の血流速度と血管抵抗の出生後変化	岩手医学雑誌	65 (5)	315 - 322	2013

Kawamura M, Ohno S, Naiki N, Nagaoka I, Dochi K, Wang Q, Hasegawa K, Kimura H, Miyamoto A, Mizusawa Y, Itoh H, Makiyama T, Sumitomo N, Ushinohama H, Oyama K, Murakoshi N, Aonuma K, Horigome H, Honda T, Yoshinaga M, Ito M, Horie M.	Genetic background of catecholaminergic polymorphic ventricular tachycardia in Japan.	Circ J.	77 (7)	1705 - 1713	2013
Yaegashi Y, Nishida J, Oyama K.	Gouty tophus of the second metacarpal simulating a malignancy with pathologic fracture.	J Hand Surg Am.	38(1)	208-209	2013
Oyama K, Chida S, Sawai T, Akio I, Fujino Y, Fujii H, Takagi M	Real-time mobile telemedicine using scalable video coding for neonatal heart disease.	Internatinoal forum on infection surveillance 2013 Morioka Japan			2013
早田航、小山耕太郎	古くて新しい心臓病-先天性心疾患-Fallot四徴症	成人病と生活習慣	43	212-217	2013
中野智、小山耕太郎	成人期の心室中隔欠損症-短絡率だけが手術適応を決めるのか	心エコー	14	54-59	2013
Tahara T, Yamamoto E, Madireddi P, Suzuki H, Maruyama R, Chung W, Garriga J, Jelinek J, Yamano HO, Sugai T, Kondo Y, Toyota M, Issa JP, Estecio MR	Colorectal Carcinomas With CpG Island Methylator Phenotype 1 Frequently Contain Mutations in Chromatin Regulators.	Gastroenterology	146 (2)	530 - 538	2014
Morino Y, Ako J, Kobayashi M, Nakamura M	Japanese postmarketing surveillance of clopidogrel for patients with non-ST-segment-elevation acute coronary syndrome indicated for percutaneous coronary intervention (J-PLACE NSTE-ACS).	Cardiovascular intervention and therapeutics.	29 (2)	123 - 133	2014
Nakano S, Oyama K, Matsuno M, Tanaka R, Yoshioka K, Nasu Y, Soda W, Takahashi S, Ikai A, Chida S	Evaluation of anomalous pulmonary venous return using 320-row ultidetector computed tomography.	J Iwate Med Assoc		in press	2014
Toya Y, Oyama K, Matsumoto A, Kusano S, Shirasawa S, Konishi Y, Sotodate G, Kasai T, Chida S	Cerebral, renal and muscular tissue oxygenation indices in preterm infants.	J Iwate Med Assoc		in press	2014
小山耕太郎	動脈管開存症	こどもケア	9	28 - 32	2014

書籍

著者氏名	論文タイトル名	書籍全体の編集者名	書籍名	出版社名	出版地	出版年	ページ
小山耕太郎	修正大血管転位症	竹中克、戸出浩之編	心エコーハンドブック・先天性心疾患	金芳堂	京都	2013	158 - 171
小山耕太郎	成人期の先天性心疾患:修正大血管転位症	新垣義夫、深谷隆	新・心臓病プラクティス	文光堂	東京	2012	244-249
中居賢司	心磁計および多チャンネル心電計	井上　博、村川祐二	不整脈学	南江堂	不明	2012	不明

Ⅵ. 研究成果の刊行物・別刷

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Original Article

World's first telepathology experiments employing WINDS ultra-high-speed internet satellite, nicknamed "KIZUNA"

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Abstract

Background: Recent advances in information technology have allowed the development of a telepathology system involving high-speed transfer of high-volume histological figures via fiber optic landlines. However, at present there are geographical limits to landlines. The Japan Aerospace Exploration Agency (JAXA) has developed the "Kizuna" ultra-high speed internet satellite and has pursued its various applications. In this study we experimented with telepathology in collaboration with JAXA using Kizuna. To measure the functionality of the Wideband InterNet working engineering test and Demonstration Satellite (WINDS) ultra-high speed internet satellite in remote pathological diagnosis and consultation, we examined the adequate data transfer speed and stability to conduct telepathology (both diagnosis and conferencing) with functionality, and ease similar or equal to telepathology using fiber-optic landlines. **Materials and Methods:** We performed experiments for 2 years. In year 1, we tested the usability of the WINDS for telepathology with real-time video and virtual slide systems. These are state-of-the-art technologies requiring massive volumes of data transfer. In year 2, we tested the usability of the WINDS for three-way teleconferencing with virtual slides. Facilities in Iwate (northern Japan), Tokyo, and Okinawa were connected via the WINDS and voice conferenced while remotely examining and manipulating virtual slides. **Results:** Network function parameters measured using ping and Iperf were within acceptable limits. However; stage movement, zoom, and conversation suffered a lag of approximately 0.8 s when using real-time video, and a delay of 60-90 s was experienced when accessing the first virtual slide in a session. No significant lag or inconvenience

was experienced during diagnosis and conferencing, and the results were satisfactory. Our hypothesis was confirmed for both remote diagnosis using real-time video and virtual slide systems, and also for teleconferencing using virtual slide systems with voice functionality. **Conclusions:** Our results demonstrate the feasibility of ultra-high-speed internet satellite networks for use in telepathology. Because communications satellites have less geographical and infrastructural requirements than landlines, ultra-high-speed internet satellite telepathology represents a major step toward alleviating regional disparity in the quality of medical care.

Key words: KIZUNA (絆), optical fiber, real-time video system, telepathology, ultra-high-speed internet satellite, virtual slide system

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INTRODUCTION

Telepathology (remote pathological diagnosis system using IT equipment) was first implemented in the early 1980s,[1] and quickly spread around the world.[2-5] In Northern Europe, it connected far northern hospitals with urban facilities. Likewise, hospitals in mountainous regions of Germany and Switzerland were connected with urban hospitals by telepathology systems.[6] In the United States, telepathology was applied to connect larger hospitals with their branches.[7,8] Telepathology has numerous applications, including consultation, intraoperative diagnosis, distance education, and conferencing. In Japan, where there are only 14 pathologists per 100,000 people and many hospitals do not have a pathologist on staff, the primary use of telepathology is overwhelmingly intraoperative remote diagnosis. This usage has received governmental support as a method to alleviate regional disparity in medical care. For this reason, great effort has been made to disseminate virtual slides.[9,10] Telepathology was initially adopted in Japan in the early 1990s. Since this time, technological advances have transformed telepathology. Analog lines were used at first.[11] Now, digital lines are used for static robotic telepathology, and fiber-optic lines transfer real-time high-definition video and virtual slide data.[12,13] Because the diagnosing pathologist can select and move the microscope's stage remotely, as well as adjust both zoom and focus using real-time high-definition video, these new technologies allow most quick diagnoses to be completed within 10 min, provided that the client and diagnostic facilities are connected by fiber-optic network. This means that telepathology can now respond to the need for intraoperative additional resection, making it almost identical to onsite pathological diagnosis at facilities with a full-time staff pathologist. The same conditions are necessary for virtual slides, which are rapidly being adopted.

Conversely, as the rapid technological development of telepathology has increased the amount of data transfer required, feasibility is increasingly limited to facilities linked via a fiber-optic network. Satellite technology, which can achieve universal coverage far more easily than landlines, is necessary to expand the use of telepathology worldwide. However, until now satellites have been weather-dependent, and prone to choppy image and video transmission. In Japan, the use of ultra-high-speed internet satellites – achieving speeds equal to fiber-optic landlines – is being promoted in various fields, including medicine.[14,15] The primary advantage of satellite technology is that, unlike landlines, communication is less limited by distance and infrastructure; it is easy to communicate via satellite with mountainous areas, remote islands, and foreign facilities unreachable by fiber-optic landlines. Ultra-high-speed internet satellite technology could alleviate regional disparity in the quality of medical care by making it possible to perform intraoperative diagnosis, consultation, and distance education with high-resolution pathological images and video.

With the support of the Research and Development Bureau of the Ministry of Education, Culture, Sports, Science, and Technology (MEXT); we tested the satellite telepathology capabilities of the Wideband InterNet working engineering test and Demonstration Satellite (WINDS), which is also known by the nickname "KIZUNA."

MATERIALS AND METHODS

Experiments were carried out over a period of 2 years. Year 1's experiments tested the interface between the WINDS and telepathology equipment, including operability and image quality for enabling optimal diagnosis The two campuses (Uchimaru and Yahaba) of Iwate Medical University (IMU), which are separated by 12 km, were connected using the WINDS to transfer real-time video images for telepathology. Results were compared to those obtained over a fiber-optic connection. In the second year, IMU was connected with Tokyo (530 km) and Okinawa (2,000 km). We evaluated the functionality and usability of remote voice conferencing for pathological diagnosis using virtual slides. Image transfer and audio functions were included.

Equipment

WINDS

An ultra-high-speed internet satellite capable of data transfer rates far exceeding existing commercial satellites.

The latter reached upload and download maximum speeds of 2 and 10 Mbps, respectively. In contrast, the WINDS reaches over 155 Mbps, or more than 15 times the speed of current commercial satellites. The WINDS' coverage is also noteworthy, reaching all of Japan and the major cities of Asia with a fixed antenna. This single satellite can communicate with points on nearly one-third of the globe, with minimal geographical limitations with a beam-hopping antenna [Figure 1].

Warp Scope

A real-time remote microscope diagnostic system. The diagnostic facility can remotely adjust focus, zoom, and stage position in real-time. Used for remote intraoperative pathological diagnosis and cytodiagnosis over fiber-optic lines. Video transmission uses WarpVision.

Specifications

Real-time remote microscope diagnostic system developed by Finggal Link Co., Ltd. (Tokyo, Japan). Image size: 1920 × 1080 at 30 fps. Objective lenses: ×1.25, ×2.5, ×5, ×10, ×20, ×40, ×63. Control: X, Y stage movement, Z focus movement. Light adjustment: Condenser.

WarpVision

A video communication service (or software) developed and trademarked by NTT Communications (Tokyo, Japan). The standard resolution version encodes and transfers 8 Mbps of video data at 640 × 480 (30 fps). The high-definition version encodes and transfers 16 Mbps of video data at 1920 × 1080 (30 fps). Video and audio delay is less than 200 ms in both versions, making conversation and remote operation smooth.

Virtual Slides

Created by digitally scanning glass slides as high-resolution digital images using a digital scanning system for the purpose of medical digital image analysis. When viewed on a computer with image management software, zoom, viewing area, etc., can be adjusted as with a microscope. Maximum optical zoom is limited by image resolution.

Virtual Slide-Related Products

ScanScope CS2 eSlide capture device and Spectrum software for digital slide management, and ImageScope viewing software (Aperio Technologies, Vista, CA, USA). Conferencing functions, including screen sharing, field movement, zoom, and annotation were tested.

Evaluated Items

This series of experiments evaluated the communications network, operability of the remote medical equipment, and the feasibility of remote diagnosis with pathological images.

Communications Network

Communication quality and maximum transfer speeds were evaluated on the WINDS experimental network, including earth stations (terrestrial terminal stations used for telecommunication with satellites and/or spacecraft, or to receive radio waves from astronomical sources). Earth stations were established at Iwate Medical University, the International University of Health and Welfare (IUHW) Mita Hospital (Tokyo), and the University of the Ryukyus (Okinawa). Figures 2a and b illustrates the conferencing network setup used in 2nd year of experimentation.

Operability of Remote Medical Equipment

We examined the interface between the WINDS and telepathology equipment (real-time video and virtual slide systems) and the operability of this system as a whole. In year 1, the communication quality of the WINDS was compared with that of land-based fiber-optic networks.

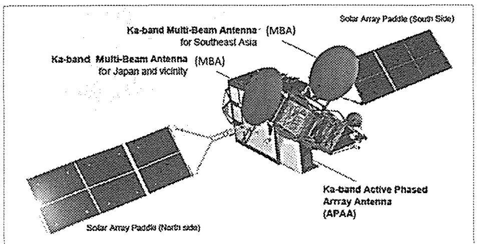

Figure 1: WINDS diagram. WINDS is a geostationary communications satellite with two solar array paddles, multi-beam antennas covering Southeast Asia with 19 fixed-spot beams, and active phased array antennas covering the Asia-Pacific region with two scanning spot beams

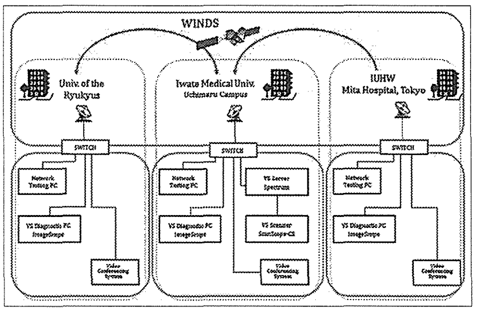

Figure 2a: Network diagram. Earth stations were placed in the three participating institutions in (Iwate Medical University, Iwate; IUHW Mita Hospital, Tokyo; University of the Ryukyus, Okinawa). Additionally, a scanner and server were placed at IMU. IUHW Mita Hospital and the University of the Ryukyus acted as client institutions and IMU as the consulting hospital

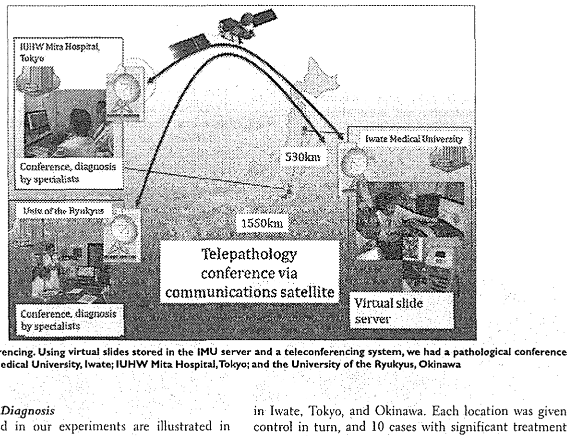

Figure 2b: Conferencing. Using virtual slides stored in the IMU server and a teleconferencing system, we had a pathological conference between Iwate Medical University, Iwate; IUHW Mita Hospital, Tokyo; and the University of the Ryukyus, Okinawa

Remote Image Diagnosis

The cases used in our experiments are illustrated in Tables 1 and 2. In year 1, we examined whether or not *Helicobacter pylori* (*H. pylori*) were identifiable with both standard and high-definition images. In year 2, three-way conferencing was tested between institutions in Iwate, Tokyo, and Okinawa. Each location was given control in turn, and 10 cases with significant treatment implications were examined. These cases included cytodiagnosis, a bone marrow smear, HER2 protein expression in breast cancer, and others of interest in targeted therapy.

Table 1: Year 1 cases

Procedure	Clinical diagnosis	Purpose
Gastric biopsy, H and E stain	Gastritis	Diagnosis and determination of histological characteristics
Gastric biopsy, Giemsa stain	Gastritis	Diagnosis and confirmation of *H. pylori* infection
Gastric biopsy, H and E stain	Gastric polyp	Diagnosis, confirmation of histological characteristics
Colon biopsy, H and E stain	Colitis	Diagnosis, confirmation of histological characteristics
Colon biopsy, H and E stain	Colon cancer	Diagnosis, histological typing
Lung biopsy, H and E stain	Lung cancer	Diagnosis, histological typing for therapeutic implications
Stomach biopsy, H and E stain	Stomach cancer	Diagnosis, histological typing
Rectal biopsy, H and E stain	Rectal cancer	Diagnosis, histological typing
Rectal surgical material, IHC (CEA)	Rectal cancer	CEA expression, and IHC confirmation of positive area

H and E: Hematoxylin and eosin, IHC: immunohistochemistry, CEA: carcinoembryonic antigen. Pulmonary and gastric tissue: Histological differentiation of pulmonary tissue made in relation with treatment. H. pylori: H. pylori positively identified. High-definition telepathological images were used because H. pylori is difficult to identify at standard resolution. Colon cancer immunostaining: Stainability of cancerous and non-cancerous areas of a single specimen was compared using carcinoembryonic antigen (CEA) to discriminate tumor and none tumor

Table 2: Year 2 three-way conferencing

Subject	Context/content	Purpose	Therapeutic implications
Lung surgical material H and E	Frozen section	Quick diagnosis classification of lung cancer	Determination for surgical procedure
Esophagus surgical material H and E	Frozen section	Quick diagnosis tumor residue in surgical margin	Determination for further excision
Thyroid gland surgical biopsy H and E	Parfaffin section	Cancer or not from nuclear properties	Selection of treatment
Bone marrow smear Giemsa	Blood smear	Nucleus/cytoplasmic features associated with leukemia	Selection therapeutic procedure
Lung cytological diagnosis papanicolau	Cytological specimen	Malignant or not cytoplasm and nuclei	Determination for therapy
Breast biopsy H and E	Paraffin section	Difficult case intraductal or extraductal invasion	Selection for surgical therapy
Mammary gland surgical biopsy H and E	Paraffin section IHC (HER2)	Score of HER2 protein, for therapy	Determination of hormonal therapy
Skin biopsy H and E	Paraffin section IHC (Ki-67)	Number of Ki-67, proliferative marker for malignancy	Selection for therapy high
Lymph node biopsy H and E, IHC	Paraffin section IHC	Monoclonality of lymphocytic tumor	Selection of therapy as plasmacytoma
Lymph node biopsy H and E	Consultation of lymph node granuloma	Classification of granuloma	Selection of therapy against tuberculosis

We examined 10 cases requiring histo- and cytodiagnosis. The specimens tested included tissue from the surgical margin (1, 2), difficult conventional histological diagnosis (3, 6, 10), a bone marrow smear (4), cytological diagnosis (5), and therapeutic uses of IHC (7, 8, 9). Samples included systemic organs; staining and evaluation procedures and treatment options vary by case

RESULTS

Communication Network

Communication Quality

We used standard network testing tools (ping and Iperf) to evaluate communication quality using the WINDS. As shown in Table 3, round-trip time (RTT) averaged 780 ms during year 1 and 800 ms in year 2. These values are in the expected normal range for the WINDS communication network. Iperf measurements of bitrate, loss, and jitter indicated normal communication quality [Table 4].

Maximum Speed

As shown in Table 5, in year 1, Iperf measured maximum data transmission rate (without application equipment attached) at 38.3 Mbps. In year 2, maximum speed was measured at 19.1 Mbps in all legs of the Iwate-Tokyo-Okinawa three-way conferencing.

Comparison with Fiber-Optic Network

As shown in Table 6, the data loss rate for communications on fiber-optic landlines was measured at a stable 0%. The WINDS experienced negligible packet loss, and error correction ensured minimal frame dropping. The WINDS achieved stable video transmission of 16 Mbps at roughly 30 fps. Video and audio packet jitter was significantly greater using the WINDS than the fiber-optic connection, but was found to be within normal values for its application mode.

Table 3: RTT measured with ping

	Sender→Receiver	Minimum	Mean	Maximum
Year 1 2010.1.27				
1 hop	Uchimaru→Yahaba	740.471	781.413	819.152
	Yahaba→Uchimaru	740.807	779.588	818.951
Year 2 2011.6.30				
1 hop	Iwate→Tokyo	746.813	786.608	825.848
	Tokyo→Iwate	756.958	794.970	836.155
	Iwate→Okinawa	746.982	785.855	824.997
	Okinawa→Iwate	775.997	811.766	854.027
2 hop	Tokyo→Okinawa	1576.921	1604.343	1625.646
	Okinawa→Tokyo	1535.765	1572.741	1614.639

ping: A network administration utility to test host reachability and measure RTT. RTT: Round-trip transmission time between the origin and terminal points of a signal, in this case between the satellite and earth stations. Hop: An excursion from one earth station to another via a communications satellite. 1 hop: Earth Station A → satellite → Earth station B. 2 hops: Earth station A → satellite → earth-based relay station → satellite → Earth station B

Table 4: Iperf results

	Client→Server	Bitrate (Mbps)	Time (s)	Loss	Jitter (ms)
Year 1	Uchimaru→Yahaba	29	60.0	0	0.604
2010.1.27	Yahaba→Uchimaru	29	60.0	0	14.253
Year 2	Iwate→Tokyo	14	60.2	0	15.621
2011.6.30	Tokyo→Iwate	14	60.3	0	18.354
	Iwate→Okinawa	14	60.0	0	1.210
	Okinawa→Iwate	14	60.2	0	15.959

Iperf: A network testing tool with parameters adjustable to measure packet transmission rates, bandwidth, etc. Loss: Packet loss (%) measured by Iperf. Jitter: Data transmission latency (delay) variation

Table 5: Maximum measured transfer speeds

	Client→Server	Bitrate (Mbps)	Time (s)	Loss
Year 1	Uchimaru→Yahaba	38.3	60.0	0
2010.1.27	Yahaba→Uchimaru	38.3	60.0	0
Year 2	Iwate→Tokyo	19.1	61.2	0
2011.6.30	Tokyo→Iwate	19.1	61.2	0
Max. transmission rate: 19.5 Mbps	Iwate→Okinawa	19.1	60.7	0
	Okinawa→Iwate	19.1	61.2	0

The maximum transmission speed of the WINDS communication network system is the nominal 155 Mbps. However, the earth station used in this experiment was limited to 51 Mbps. In this case, the effective rate was about 38 Mbps (about 70% of the nominal rate). Year 1 connected client and diagnostic facilities directly; the effective transmission rate was 38 Mbps. Year 2 connected client and diagnostic facilities through Tokyo, halving the effective transmission rate

Table 6: Comparison of the WINDS with fiber-optic network

	WINDS		Fiber-optic landline	
	Yahaba→Uchimaru	Uchimaru→Yahaba	Tokyo→Okinawa	Okinawa→Tokyo
Transmission rate (kbps)	16043	16021	1675	929
RTT (ms)	821.78		43.16	
Loss (%)	0.334	0.42	0	0
Video packet jitter (ms)	14.87	14.42	1.71	0.95
Audio packet jitter (ms)	14.7	13.65	1.62	0.87
Measurement time (s)	46		428	

The above data was calculated from packets captured by logging tools installed in the client computers at each transmission terminus. In application mode, the WINDS uses WarpVision HD (full high definition = 1920×1080) while the fiber-optic network uses WarpVision (QVGA = 320×240). The transmission rate disparity reflects the resolution differences

Operability of Remote Medical Equipment

WarpVision Real-time Video System (Year 1)

For diagnosis to be made, remote microscopy requires manipulability of the field of vision, zoom, and focus. Overall, the functionality of high-definition image manipulation presented no significant difficulty and was comparable to that with a fiber-optic connection, though the focus lagged approximately 0.8 s.

Virtual Slides (Year 2)

We accessed the Spectrum digital slide management server and confirmed that virtual slides were viewable. The virtual slide images were dithered (displayed as a low-resolution mosaic) while loading, and took approximately 1 min to fully load. Once completely loaded and displayed at full resolution, no inconvenience was experienced in adjusting the field of vision or zoom. Additionally; shape, stainability, and some level of microstructure were observable.

Pathological Image Cases

Year 1 Cases

Gastric Cancer Biopsy

A biopsy containing both undifferentiated carcinoma and normal tissues was compared. Cellular characteristics of the invasive cancer cells with significant atypia were clearly confirmed and diagnosis was possible with no difficulties.

H. pylori Confirmation

Identification of *H. pylori* is difficult with standard-definition images, but not with the high-definition images used in these experiments. *H. pylori* were confirmed with both Giemsa and hematoxylin and eosin (HE) staining, as shown in Figure 3.

Colon Cancer Immunostaining

The cancerous area exhibited brownish-red color indicating positive reaction to the antibody, while the noncancerous area was negative.

Lung Tissue

Cancerous and normal cells were easily distinguishable on the basis of histo- and cytological findings such as cytoplasmic anomalies, nuclear atypia, and chromatin coarseness.

Year 2 Cases

We accessed the digital slide server at IMU from two remote points (IUHW Mita Hospital, Tokyo and University of the Ryukyus, Okinawa) and viewed virtual slides. The results of conferencing conducted via the *WINDS are summarized below.*

Lung Tissue

Tissue sample excised from a lesion from an abnormal chest X-ray shadow. Consultation requested to diagnose and determine treatment. Diagnosis according to Noguchi's classification type A of adenocarcinoma,[16] required focal rather than extended resection lobectomy or radical lymph dissection (lymph adenectomy). (IMU case.)

Esophageal Tissue

Consultation on pathological diagnosis revealed cancer remaining in the marginal region. Additional resection required. No relapse at the time of writing. [Figure 4; IMU case]

Thyroid Tissue

Consultation on malignancy for postoperative histological specimen. Nuclear grooves and inclusion bodies identified, and diagnosed as papillary adenocarcinoma (follicular variant); total thyroidectomy performed with radical dissection of cervical lymph nodes [Figure 5; University of the Ryukyus case].

Bone Marrow Smear

Diagnosis of smeared slide with suspected hemopathies, including leukemia. Images at ×20 magnification insufficient to identify nuclear and cytological characteristics necessary for diagnosis; ×40 images required instead. Diagnosed as benign. (IMU case.)

Pulmonary Cytodiagnosis

Cellular and nuclear characteristics and cellular alignment and overlap are considered diagnostic indicators of malignancy. Cytodiagnosis is methodologically simpler than histodiagnosis. This case diagnosed as pulmonary adenocarcinoma based on nuclear atypia and size variation, increased chromatin levels, and cellular overlap. The ×20 images were diagnostically sufficient. However, cytodiagnosis found to require rapid focus adjustment [Figure 6; IMU case].

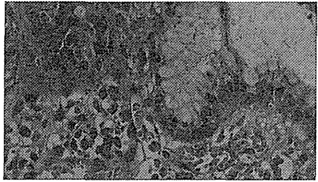

Figure 3: Giemsa staining *Helicobacter pylori* were visible, with club-shaped figures (25.5 μm in length). *H. pylori* is implicated in the genesis of stomach cancer and malignant lymphoma (arrows)

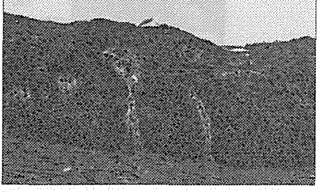

Figure 4: Esophageal tissue specimen. Additional excision was performed for esophageal carcinoma because of atypical cell residue on the surgical margin

Mammary Gland

Difficult case of suspected invasive breast cancer. Primarily intraductal, but slight extraductal invasion confirmed. Only local tumor resection and close follow-up required (IUHW case.)

Mammary Gland

Scoring of immunohistochemical HER2 reactivity for selecting antibody therapy [Figure 7]. Recently, targeted antibody therapy has joined the regimen of resection and chemotherapy. Immunohistochemistry (IHC) is used for scoring the amount of HER2 protein, and selecting appropriate treatment. Three samples were immunostained and scored at each facility. All diagnoses matched; two were categorized as score 3, and one as score 2. This sample was referred for fluorescence *in situ* hybridization (FISH). (IUHW case.)

Skin Biopsy

Suspected benign dermatofibroma of the forearm. However, cellular density and nuclear characteristics indicated possible malignancy. Sample immunostained with cellular proliferation marker ki-67. Unable to rule out malignancy despite low ki-67-positive cell count. All three facilities agreed on need for additional immunostaining with CD34 or consultation with dermatopathologist. (IMU case.)

Lymph Node Biopsy

Swelling of lymph node with cell proliferation, characterized by cell shape and nuclear position. Additionally, immunohistochemical staining demonstrated only κ-chain immunoglobulin-positive cell proliferation, led to diagnosis as kappa-type plasmacytoma. Cellular characteristics and positive immunostaining observable and acceptable to all conferencing participants. (University of the Ryukyus case.)

Lymph Node

Swelling of lymph node diagnosed as noncancerous sarcoidosis. Granuloma in this case characterized by little confluence and necrosis. (University of the Ryukyus case.)

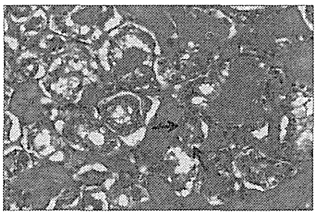

Figure 5: Thyroid tissue specimen. Thyroid tumor: Diagnosis was papillary carcinoma (follicular variant) with nuclear grooves

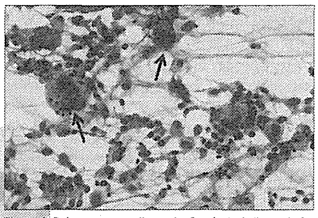

Figure 6: Pulmonary cytodiagnosis. Cytological diagnosis for sputum: Adenocarcinoma with cluster formation composed of many atypical cells

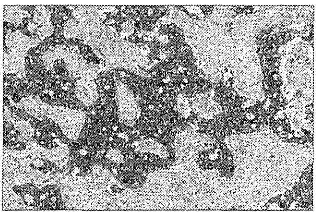

Figure 7: Mammary gland specimen. The patient received antibody therapy based on the result of immunohistochemical score 2 reactivity for HER2 protein

DISCUSSION

The WINDS is one of many Japanese satellites. In addition to communications, satellites are used for weather forecast, disaster prevention, and numerous other purposes in Japan.[17] The WINDS was developed by the Japan Aerospace Exploration Agency (JAXA) and the National Institute of Information and Communications Technology (NICT) in order to overcome the digital divide and provide universal broadband internet service. The satellite is nicknamed "Kizuna" ("connection," or "human bond" in Japanese), a word which has special resonance after the earthquake and tsunami of March

11, 2011. The WINDS is still experimental, but potential uses include industrial, scientific and educational services, as well as to provide information for use in disaster prevention. The WINDS is distinguished by a combination of mobility, wide coverage area, and robustness in the event of disaster. It provides higher data transfer speeds using smaller antennas than existing communications satellites. Portable user terminals receive 155 Mbps with 45 cm aperture antennas and transmit 155 Mbps with 1.2 m antennas. Terminals of this size are easily transportable anywhere within the satellite's coverage area. The WINDS has fixed antennas for Japanese and major southeastern Asian cities, and high-speed scanning antennas that provide total coverage of nearly one-third of the globe without reliance on landline infrastructure. This means that if a natural disaster interrupts land-based networks, portable the WINDS terminals can easily be transported into affected areas and easily set up alternative network service. For instance, after the disaster of March 11, 2011, the WINDS mobile earth stations were installed at the Iwate Prefectural Office and the affected coastal cities of Kamaishi and Ofunato, allowing high-definition videoconferencing and internet access.[18] These characteristics mean that, unlike fiber-optic cable networks, the WINDS can provide service in mountainous regions and isolated islands. The WINDS uses an ethernet connection, making it highly compatible with land-based internet networks. The WINDS and landlines can be used complementarily to create more reliable networks. The success of these telepathology experiments indicates that the WINDS interface is well adapted for remote medical services. In the future, it is expected that the WINDS will be used to provide telemedicine services and medical cooperation for the Asia-Pacific region.

Japan has numerous public and private communications satellites in use [Table 7], but the WINDS is capable of data transmission speeds far outstripping any of them. Because telepathology requires the transfer of very large amounts of data, it is highly unlikely that any other available satellite could achieve the image quality and stability necessary for telepathology.

Virtual slides require more preparation (scanning) time than real-time video, but once prepared and saved to a server, they are accessible from anywhere.[19,20] Virtual slides are used around the world in educational settings; according to Weinstein, students at Arizona University use virtual slides exclusively, completely discarding optical microscopy.[1] The Japanese Ministry of Health, Labor, and Welfare (MHLW) has helped fund the purchase of about 250 scanners nationwide for the "standardization of cancer medical services". Throughout the country, 60% of medical schools have introduced virtual slides, and 20% of facilities with virtual slide capability use them in lectures and practice.[21]

WarpScope is a dynamic robotic telepathology system capable of real-time video function.[13] The diagnostic pathologist can select the visual field freely and control the focus of microscope in a user environment almost identical to a traditional optical microscope. Recently, high-definition equipment has been developed. We used high-definition images in WarpScope via WINDS to identify *H. pylori* (2.5-5 μm) bacteria, which are associated with occurrence of gastritis and gastric cancer.

In the first year of this series of experiments, we performed pathological diagnosis using a robotic microscope with real-time video. In the second year, we confirmed that three-way conferencing using virtual slides was feasible via a WINDS connection. Network parameters measured with ping and Iperf were normal, but stage movement, zoom, and conversation suffered a lag of approximately 0.8 s. A delay averaging 60-90 s was experienced when initially accessing virtual slides saved to the server. When one participant changed the objective field significantly, there was a delay of 10-15 s before the slide image was reloaded at the other two sites. Jitter using the WINDS network ranged from 0.604 to 14.253 ms. During loading, images were mosaicked. This phenomenon was unusual when using a fiber-optic network, and may have been due to weather conditions.

No direct connection was established between Tokyo and Okinawa for three-way conferencing. Therefore, communication between these two points required two hops (sender-satellite-Iwate-satellite-receiver). As a result, RTT was nearly doubled [Table 3] over single hop connections, resulting in image and voice transmission delays. This is characteristic of communications satellites.

Conferencing was highly successful. We were able to manipulate the images as we conversed, and all participants reached consensus on histopathological findings; including nuclear shape, cellular characteristics, and structure; and immunostaining results. Our results indicate that, for both educational and pathological applications, WINDS could serve as an effective substitute when and where fiber-optic networks are not available. There are many possible uses for the WINDS. We expect that in the future, WINDS will also be used to communicate with foreign facilities. In addition to consulting with hospitals in the United States and Europe, it should be possible to assist with diagnosis, training, and quality control in Southeast Asia.[22] A high-speed broadband satellite like WINDS could service areas unreached or unreachable by fiber-optic networks (mountainous and desert regions, and isolated islands) resulting in tremendous medical advancements for mankind.

CONCLUSION

These experiments demonstrate that the WINDS ultra-high-speed internet satellite is suitable both for

Table 7: Japanese communications satellites

Satellite (band)	Service (provider)	Domestic users	Fixed/ transportable	Size	Output	Weight	Transfer speed (bps)	Interface
WINDS (Ka)	Ultra-high-speed internet (JAXA/ NICT)	N/A	Fixed/ Transportable (Loan)	120 cm	40 wSSPA	90 kg	1-155 M	RJ-45 Router and TCP accelerator connection
ETS-VIII (S/Ka)	Engineering test satellite (JAXA/ NICT)	N/A	Fixed/Mobile (Loan)	285×374× 125 mm 28.5×78× 174.5 mm		8.2 kg 300 g	Voice: 5.6 k Data: 32 k Packets: 1024 k Broadcast: 220 k×6 cH	140 MHz band IF I/O RJ-45 Ethernet
Thaicom-4 (Ku/Ka)	IPSTAR internet service (IPSTAR Co., Ltd.)	IPSTAR Co., Ltd.	Fixed c. 150,000 yen (+ installation fee)	120 cm/ 84 cm	1 w	20 kg /10 kg	Home: 1 M/512 k Flex: 2 M/1 M Dual: 2 M/2 M Pro: 3 M/1 M Biz: 4 M/2 M	RJ-45
Inmarsat (L)	BGAN (Inmarsat)	KDDI Softbank JSAT Mobile Japan Digicom	Fixed/ Transportable (Car-/ship-mountable) EX500: c. 400,000yen ea. EX700: c. 700,000yen ea.	Explorer500 218×217× 52 mm Explorer700 297×339× 51 mm	14 w 14 w	1.5 kg 3.2 kg	Voice: ISDN: 64 k Packets: 492 k Streaming: 128-256 k	Ethernet, USB, Bluetooth Ethernet, wireless LAN, USB, Bluetooth
N-Star (S)	Widestar II (NTT Docomo)	NTT Docomo	Fixed/ Transportable (Car-/ship-mountable) c. 370,000yen	Flat-panel antenna 197×180× 39 mm	2w	1.3 kg	Streaming: 8 k Data: (Packets: 384 k) (64 k data: 64 k)	RJ-45
JCSAT (Ku-band)	ExBird (SKY Perfect JSAT)	SKY Perfect JSAT SNET	Fixed/ Transportable c. 480-680,000 yen ea. Rental: 160,000yen	75 cm	2 w		Internet service Premier: 8M/ 1.2 M Standard: 4 M/400 k	RJ-45 10/100Base-T (Ethernet)
JCSAT (Ku)	PortaLink (SKY Perfect JSAT)	SKY Perfect JSAT	Mobile c. 10 million yen ea.	Flat-panel antenna 744×649× 860 mm	25 WSSPA	20 kg	3 M/1.5M 6M/1.5M 9M/1.5M (HD-capable)	RJ-45 10/100Base-T
Inmarsat (L)	Isat Phone Pro (Inmarsat)	JSAT Mobile NTT Docomo KDDI Japan Digicom	Mobile phone c. $600 ea.	54×170× 39 mm		279 g	Voice: Voicemail: SMS: Data: 2.4 k	Bluetooth 2.0 Micro SD Audio socket Antenna port
Iridium (L)	Iridium 9555 (Iridium)	KDDI Japan Digicom	Mobile phone c. 250,000 ea.	30×55× 143 mm	0.57 w	266 g	Voice: Data: 2.4 k Packets:	miniUSB
Thuraya-3 (L)	Thuraya	Softbank (Limited area)	Mobile phone (w/GSM) c. $500 ea.	53×128× 26.5 mm		193 g (w/battery)	Voice: IP data: 384 k	Data Cable (UDC) with USB connector

This table indicates that the data transmission rates achieved by the WINDS are very high in comparison to those of Japanese R and D, engineering, and commercial satellites currently in service

pathological diagnosis with real-time video and for viewing and manipulating still-image virtual slides for conferencing and consultation. These results indicate that in the future, Japan's WINDS could be used internationally for microscopic image diagnosis, education, and research.

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REFERENCES

1. Weinstein RS, Graham AR, Richter LC, Barker GP, Krupinski EA, Lopez AM, *et al.* Overview of telepathology, virtual microscopy, and whole slide imaging: Prospects for the future. Hum Pathol 2009;40:1057-69.
2. Scoville SA, Buskirk TD. Traditional and virtual microscopy compared experimentally in a classroom setting. Clin Anat 2007;20:565-70.
3. Harris T, Leaven T, Heidger P, Kreiter C, Duncan J, Dick F. Comparison of a virtual microscope laboratory to a regular microscope laboratory for teaching histology. Anat Rec 2001;265:10-4.
4. Weinstein RS, Bhattacharyya AK, Graham AR, Davis JR. Telepathology: A ten-year progress report. Hum Pathol 1997;28:1-7.
5. Weinstein RS, Descour MR, Liang C, Bhattacharyya AK, Graham AR, Davis JR, *et al.* Telepathology overview: From concept to implementation. Hum Pathol 2001;32:1283-99.
6. Kayser K, Szymas J, Weinstein RS. Telepathology in Europe. In: Kayser K, Szymas J, Weinstein RS, editors. Telepathology: Telecommunication, Electronic Education, and Publication in Path, 1st ed. Heidelburg: Springer Verlag; 1999. p. 113-22.
7. Ferreira R, Moon B, Humphries J, Sussman A, Saltz J, Miller R, *et al.* The virtual microscope. Proc AMIA Annu Fall Symp 1997:449-53.
8. Dunn BE, Almagro UA, Choi H, Recla DL, Weinstein RS. Use of telepathology for routine surgical pathology review in a test bed in the Department of Veterans Affairs. Telemed J 1997;3:1-10.
9. Sawai T. Telepathology in Japan. In: Kumar S, Dunn BE, editors. Telepathology. 1st ed. Heidelburg: Springer Verlag; 2009. p. 105-26.
10. Murakami K. Applications of virtual slides via the internet. In: Sawai T, editor. Telepathology in Japan-Development and Practice. 1st ed. Morioka: Celc Inc; 2007. p. 206-9.
11. Sawai T, Uzuki M, Kamataki A, Tofukuji I. The state of telepathology in Japan. J Pathol Inform 2010;1. pii: 13.
12. Yamazaki T, Sawai T, Noda Y, Fujita N, Miyagawa K. Telepathology in the age of fiber optics. In: Sawai T, editor. Telepathology in Japan-Development and Practice, 1st ed. Morioka: Celc Inc; 2007. p. 77-80.
13. Kumagai K. Finggal link warpscope. In: Sawai T, editor. Telepathology in Japan-Development and Practice, 1st ed. Morioka: Celc Inc; 2007. p. 188-90.
14. Japan Aerospace Exploration Agency. WINDS Basic Experiment. Available from: http://winds-ets8.jaxa.jp/winds/en/experiments/basic/index.html [Last accessed on 2013 Jun 20].
15. Japan Aerospace Exploration Agency. KIZUNA (WINDS): Expanding the utilization of space-based, high-speed Internet. Available from: http://www.jaxa.jp/countdown/f14/overview/application_e.html [Last accessed on 2013 Jun 20].
16. Noguchi M, Morikawa A, Kawasaki M, Matsuno Y, Yamada T, Hirohashi S, *et al.* Small adenocarcinoma of the lung. Histologic characteristics and prognosis. Cancer 1995;75:2844-52.
17. Japan Aerospace Exploration Agency. Wideband InterNetworking engineering test and Demonstration Satellite "KIZUNA" (WINDS). Available from: http://www.jaxa.jp/projects/sat/winds/index_e.html [Last accessed on 2013 Jun 20].
18. Japan Aerospace Exploration Agency. Report on JAXA's Response to the Great East Japan Earthquake (Assistance using earth observation satellites and communication satellites). Available from: http://www.sapc.jaxa.jp/antidisaster/20110311report_e/311report0_e.pdf [Last accessed on 2013 Jun 20].
19. Nakayama I, Matsumura T, Kamataki A, Uzuki M, Saito K, Hobbs J, *et al.* Development of a teledermatopathology consultation system using virtual slides. Diagn Pathol 2012;7:177.
20. Rojo MG, García GB, Mateos CP, García JG, Vicente MC. Critical comparison of 31 commercially available digital slide systems in pathology. Int J Surg Pathol 2006;14:285-305.
21. Sawai T. Application of virtual slide for medical education. Jpn J Clin Exp Med (Igaku no Ayumi) 2010;234:288-91.
22. Nabandith V, Pholsena V, Mounthisone P, Shimoe K, Kato S, Aoki K, *et al.* First trial of cervical cytology in healthy women of urban laos using by self-sampling instrument. Asian Pac J Cancer Prev 2012;13:4665-7.

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Original Article

The history of pathology informatics: A global perspective

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Abstract

Pathology informatics has evolved to varying levels around the world. The history of pathology informatics in different countries is a tale with many dimensions. At first glance, it is the familiar story of individuals solving problems that arise in their clinical practice to enhance efficiency, better manage (e.g., digitize) laboratory information, as well as exploit emerging information technologies. Under the surface, however, lie powerful resource, regulatory, and societal forces that helped shape our discipline into what it is today. In this monograph, for the first time in the history of our discipline, we collectively perform a global review of the field of pathology informatics. In doing so, we illustrate how general far-reaching trends such as the advent of computers, the Internet and digital imaging have affected pathology informatics in the world at large. Major drivers in the field included the need for pathologists to comply with national standards for health information technology and telepathology applications to meet the scarcity of pathology services and trained people in certain countries. Following trials by a multitude of investigators, not all of them successful, it is apparent that innovation alone did not assure the success of many informatics tools and solutions. Common, ongoing barriers to the widespread adoption of informatics devices include poor information technology infrastructure in undeveloped areas, the cost of technology, and regulatory issues. This review offers a deeper understanding of how pathology informatics historically developed and provides insights into what the promising future might hold.

Key words: History, pathology informatics, clinical informatics, electronic medical record, laboratory information systems, pathology education

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INTRODUCTION

> "If I have seen further, it is by standing on the shoulders of giants."
>
> - Sir Isaac Newton

The history of pathology informatics is a tale with many dimensions. At first glance, it is the familiar story of individuals solving problems that arise in their clinical practice of medicine. Under the surface, however, lie powerful forces – technical, regulatory, societal and beyond – that have all played their part in molding our discipline into what it is today. In this monograph, we take – perhaps for the first time in the history of our discipline – a truly global perspective of how the field of pathology informatics has evolved. In doing so, several large-scale trends are immediately obvious. For example, the advent of computers, the Internet and digital cameras were major disruptive events that advanced the practice of pathology in many countries. The prevalence of different technologies in different regions was related to both tangible factors (e.g., availability of trained staff and operational costs) and intangible factors (e.g., regulatory concerns). Though pathology informatics was born in the USA and Europe, it is now a truly global discipline; no single country or continent can lay claim to being the sole driver of our discipline's destiny. If we are to be wise stewards of our discipline, it is necessary for us to know where we have been, not only so that we may give our pioneers and discoverers their just recognition, but also so that we can learn from the successes and failures of past decades.

The aim of this collective effort was to record the history of pathology informatics around the world. Pathology informaticists with knowledge about the field, representing virtually all of the continents, were asked to share their experience, literature, publications, archived documents and images, as well as their insights. Their contributions have been collated and divided up in this monograph by continent and presented below in alphabetical order. While an attempt was made by the authors to comprehensively capture all available detail, we acknowledge that there may be voices and events that were missed.

AFRICA

The history of pathology informatics in Africa is a story of struggle – and in many cases, triumph – against an almost overwhelming lack of infrastructure and resources. Particularly in sub-Saharan Africa, there was, and still remains, an extreme shortage of medical personnel, including pathologists. Even when medical personnel exist they are generally concentrated in the major cities. The tendency for doctors to emigrate – especially from war-torn areas in which they are arguably most needed – worsened this shortage. As a result, pathology services are often scarce and possibly below acceptable standards, especially with regard to the availability of certain laboratory tests (e.g., immunohistochemistry, molecular studies) and specimen processing. For example, in 2007 Uganda had 18 pathologists serving a population of 28 million, Tanzania had 15 pathologists serving a population of 38 million, and Sudan had 51 pathologists (40 of whom work mostly in the capital city of Khartoum) serving a population of 40 million. In Zambia, there is only one pathologist, at the University Teaching Hospital of Lusaka.[1]

It should therefore, come as no surprise that (a) Africa currently represents perhaps the greatest unmet need for pathology services in the world and (b) pathology informatics in Africa has historically focused most heavily on telepathology applications (primarily with European collaborators) to outsource their work and/or seek expert consultation.[2,3] This is especially true in countries like Sudan and South Africa, which have more pathologists as well as relatively advanced telecommunications and Internet services, and as such were positioned to better leverage multiple telepathology efforts with collaborators from other countries.[1-3] A common theme in Africa, as was the case around the world, was the transformational change in medicine that was realized as a result of the introduction of computers, coupled to networking technologies like the Internet, into healthcare.

Telepathology

In 1991, Heinz Hoenecke of the USA founded the volunteer organization called Pathologists Overseas with the express purpose of setting up and running pathology laboratories for resource-restricted nations in Africa. Emphasis was initially placed on providing pathology services where the need was greatest and on training local medical professionals to become pathologists.[4] Thereafter, when resources become available and technical limitations were overcome, this organization embraced telepathology in several African countries.[5]

In France, a private company named Réseau Internationale de Télémédecine (RESINTEL) was founded in 1992 at the University of Dijon to provide telemedicine services – with a special emphasis on telepathology – to geographically isolated areas of France. The telepathology system and international telecommunications network that it created – collectively known as TRANSPATH – together provided a platform for static telemicroscopy that was originally telephone-based, but quickly moved to Integrated Services Digital Network (ISDN) and satellite communication methods. By 1994, RESINTEL had signed contracts with – and was providing telepathology services for – hospitals in India, the Middle East, Morocco, and several countries in Africa.

Unfortunately, circa 1998 the TRANSPATH network was shut down due to the fact that RESINTEL could not secure funding for continued operation.[6]

In 1997, the Fundamentals of Modern Telemedicine in Africa (FOMTA) project developed regional networks between research centers and universities of many African countries, using up to 256 kbps ISDN connections for the store-and-forward of medical images (including static telemicroscopy) and the remote control of medical instruments. These initial efforts were limited by the lack of high-quality network infrastructure in many of the target nations and by the nascent state of network-capable collaborative editing and publication software stacks at the time, but were nevertheless successful in providing static telepathology services where none had previously existed.[7] By the mid-2000's, FOMTA – and other regional telepathology projects like it – largely migrated to open-architecture telepathology platforms written atop Linux, Apache, MySQL, PHP (LAMP) stacks, of which iPath has been the most successful in Africa (see section: Data Management Platforms).[8]

The first reports of telepathology and teleradiology services in Tunisia date from 1999. These services – primarily between hospitals in Tunis (Institut Pasteur, Hôpital de l'Enfance) and Nice (Hôpital Antoine) and Marseilles (Hôpital de la Timore) in France – focused primarily on cancer diagnoses utilizing static images. Other similar telepathology projects were developed (e.g., between the Farhat Hached Hospital in Sousse, Tunisia and several French cancer centers), which utilized videoconferencing stations for real-time presentation of cases. This was the first appearance of non-static telepathology methods in Africa.[9,10]

The year 2000 was momentous for telepathology in Africa. In Madagascar, the Pathologists Overseas laboratory adapted a commodity digital camera for use with a microscope, pairing it via Universal Serial Bus to a computer for rapid transmission of static photomicrographs over the Internet.[4] In August of that year, Dr. Agostino Faravelli of Associazione Patologi Oltre Frontiera (APOF) travelled with a microscope and a digital camera to Mwanza, Tanzania, where he enabled static telemicroscopy by E-mailing digital photographs as E-mail attachments to colleagues in various institutions in Italy. APOF subsequently established a local presence in Mwanza, which continued experimentation with telepathology methods over a 7-year period before it closed in 2007.[11] The use of static and live telemicroscopy by these pathologists was discussed with a multinational group of participants in a live online videoconference hosted by the Regional Dermatology Training Centre in Moshi, Northern Tanzania.[12]

2001 marked the startup of the Generic Advanced Low-cost trans-European Network Over Satellite (GALENOS) network, a satellite-based telecommunication infrastructure that offered 2 Mbps interfaces to participating clinics. GALENOS eventually covered a total of 14 clinics in Bulgaria, France, Germany, Greece, Italy, and Tunisia; it enabled intraoperative telepathology using a robotic microscope with a video camera and remote control capability.[2] The iPath platform for telepathology gained significant traction during this year, being extensively used by the Eastern Cape Province Department of Health in South Africa[13,14] and the Réseau Afrique Francophone de Télémédecine (RAFT) project (organized by the Geneva University Hospitals) in developing countries in Western Africa. Both of these pathology education projects delivered interactive courses and the ability for tele-consultation utilizing a single common infrastructure. The RAFT project was particularly successful, extending to 17 African countries (Mali [2001], Mauritania [2002], Morocco [2003], Burkina Faso [2004], Sengal [2004], Tunisia [2004], Cameroon [2005], Ivory Coast [2005], Madagascar [2005], Niger [2006], Benin [2006], Burundi [2007], Congo [2007], Algeria [2007], Chad [2008], Guinea [2008], and Rwanda [2008]) as of the time of the writing of this monograph.[2,15,16]

In 2002, apart from reports about the success of the long-running live telemicroscopy projects of Farhat Hached Hospital in Tunisia, other hospitals in this region such as the Aziza Othmana Hospital in Tunis also reported on their telecytology and telehematopathology projects.[10] Also in 2002, the Nkosi Albert Luthuli Central Hospital in Durban, KwaZulu-Natal (South Africa) – the first hospital in Africa designed for truly paperless operation – opened its doors, and has since been a regional champion of enabling telemedicine through the use of radiology and pathology picture archiving and communication system (PACS) systems.[17]

Another two telepathology systems – both of which have experienced enthusiastic growth to the present day – were born in 2003. The first – a pilot project between the Italian Hospital in Cairo, Egypt and the Civico Hospital in Palermo, Italy – utilized both static and video telepathology. This project has expanded to neighboring countries in recent years and is expected to continue operating into at least the near future.[18] The second telepathology system was located in a more bandwidth-limited milieu: The Kijabe Hospital in Kenya. This latter system – which currently provides telepathology services for over 50 mission hospitals throughout Africa – utilizes a microscope camera attached to a computer, permitting static photomicrographs to be E-mailed to international colleagues for consultation and diagnosis confirmation.[19]

2004 saw the advent of robotic microscopes integrating rudimentary whole slide imaging (WSI) technology in Africa. At the Allada Hospital in Benin, a Nikon Coolscope was utilized in conjunction with a broadband Internet connection to send both digitized (scanned) slides and digital static photomicrographs of selected regions of interest on glass slides to collaborators in Milan, Italy.[20] Later that year, another Nikon Coolscope was installed aboard a non-governmental hospital ship initially based in Cotonou, Benin, also for static and live telepathology applications. An onboard satellite communication system provided Internet connectivity for this system, which is still in operation in its original configuration today.[21,22] In that same year in Casablanca, Morocco, a telemedicine unit equipped with a satellite connection and four ISDN lines was deployed, utilizing a microscope with an attached digital camera for telepathology.[23] Ethiopia also made large strides in telepathology in 2004, launching a project that connected 10 regional hospitals in the country with the Tikur Anbessa Hospital and the Faculty of Medicine of Addis Ababa University. In the same timeframe, the "Ethiopia Pathology" group in iPath was organized for the purpose of providing second opinion consultations with pathologists from Switzerland and Germany. Moreover, this work has improved access to continuing education and training, raised the level of access to care and drastically reduced the waiting time and cost associated with long-distance travel by patients for diagnosis in that country.[2,24]

In 2005, APOF installed a Nikon Coolscope at the Mtendere Mission Hospital in Chirundu, Zambia, leveraging pre-existing satellite Internet connectivity and Skype (a commercial voice-over-IP videoconferencing application) to allow APOF pathologists (living in Italy) to easily provide telepathology services. This system remains popular in the present day, and has made the Mtendere Mission Hospital the definitive regional hub for pathology services within a 100 km radius.[11] Also in 2005, the Euro-Mediterranean Internet-Satellite Platform for Health, Medical Education and Research (EMISPHER) went live, providing real-time online telemedicine services with high emphasis on network quality of service to most of the countries in the Mediterranean region, including Morocco, Algeria, Tunisia, Egypt, Cyprus, Turkey, Greece, Italy, France, and Germany. EMISPHER integrates satellite Internet connectivity known as MEDSKY (up to 2 Mbps) and a custom real-time telemedicine and telepathology application known as WinVicos. It still remains considerably popular, especially in geographically isolated regions where traditional wired Internet connections may not be possible.[2]

The year 2006 marked the first appearance of modern WSI scanners in Africa. During 2006, the Euro-Mediterranean Network for Genetic Services (MedGeNet) – a European Union funded project – installed an Aperio ScanScope GL at the Hospital Charles Nicolle in Tunisia, and then used that WSI scanner to successfully validate the first ever WSI-based telepathology service in the Mediterranean region.[25] One year later, in 2007, APOF built on their already-successful efforts at the Mtendere Mission Hospital in Chirundu, Zambia, with the installation of an Aperio ScanScope CS. Digitized whole slides were stored on a local File transfer protocol server that was made accessible to Italian collaborators via the pre-existing satellite Internet connection, which had been substantially upgraded to provide sufficient bandwidth to support the upload and download of large WSI files.[11] Two pathologists, located in Italy, independently examined the scanned WSIs remotely.[26]

Of note, 2007 proved to be a landmark year for telepathology throughout the rest of Africa as well. The Africa Teledermatology Project (http://africa.telederm.org/) – which provides dermatology support to local providers throughout Africa (Uganda, Botswana, Malawi, Swaziland, Burkina Faso, and Lesotho) – began operations during this year, utilizing a platform (telederm.org) that was initially only capable of static digital gross photographs and photomicrographs. The main limitations at this time were the number and quality of images available to the remote consultant and their reliance on the referring provider, who usually lacked dermatopathology training, to provide representative photomicrographs.[17] In May 2007, a histology laboratory was created at St. Joseph's Mission Hospital Peramiho in Tanzania, but without a local practicing pathologist. iPath was therefore, used to enable telepathology at this site, utilizing static digital photomicrography to send images for diagnosis to pathologists based in Germany.[27] Also in 2007, at the Kuluva Hospital in the Arura district of northwest Uganda, a microscope eyepiece mounted Motic camera was utilized in conjunction with a laptop to E-mail static digital photomicrographs to a pathologist in Kampala, Uganda.[28,29] Finally in 2007, at the Kahuzi-Biéga National Park in the eastern Democratic Republic of the Congo, the Centre de Recherches de Sciences Naturelles, with the collaboration of the Spanish government, started a human and veterinary telepathology service utilizing a satellite Internet connection.[30]

In March of 2008, a pilot telepathology service known as Remote Access for Health Professionals was established with the objective of promoting evidence-based medicine in developing countries. An asynchronous static telepathology program was created in collaboration between four hospitals throughout Tanzania and Kenya and the Massachusetts General Hospital (MGH) (Boston, MA, USA) to provide dermatopathology consultation to local pathologists, using skin histopathology images captured by microscope-mounted digital cameras in conjunction with iPath. The authors of this work identified limitations with static telepathology that could as they posited, be overcome with increased training.[31] Later in 2008, an initiative in Ghana to use microscopes with attached digital cameras to allow quick consultations failed due to the lack of adequate bandwidth, as well as the high cost of the required equipment.[2] Finally in 2008, the Indian government initiated a project known as the Pan African e-Network (http://www.panafricanenetwork.com/). The objective of this project was to provide tele-education and telemedicine services (including all necessary medical and computer equipment) to 53 remote hospitals in Africa via satellite (International Telecommunications Satellite Organization (INTELSAT), European Telecommunications Satellite Organization (EUTELSAT), Regional African Satellite Communication Organization (RASCOM)) and fiber optic links to 12 super-specialty hospitals in India.[16]

In 2009, the French association Pathology, Cytologie, Développement (PCD) installed a telepathology service in Brazzaville, Congo, with the cooperation of the Francophone Digital University.[32] Also in 2009, a Zeiss Mirax Live RT system – a combination robotic microscope and WSI scanner – was installed in the National Health Laboratory in Gaborone, Botswana as part of the Africa Teledermatology Project.[33]

More recent telepathology events in Africa date to 2010. In this year, static telepathology was applied to vaginal cytology at the APOF projects in Zambia, Madagascar, and Tanzania for quality control purposes.[34] Also during this year, the French branch of Alliance Mondiale Contre le Cancer, International Network for Cancer Treatment and Research Programs began development of a telepathology network in sub-Saharan Africa for diagnostic, pedagogic, and research purposes, initially for lymphomas (which has now been expanded to a broad range of diseases). Partners in this endeavor were the French National Cancer Institute INCa, the PCD Association, and the Groupe Franco-Africain d'Oncologie Pediatrique. Pilot centers for telepathology have been established in the Kenyatta National Hospital in Nairobi, Kenya, in Dar-es-Salaam, Tanzania, and in Ile-Ife, Nigeria, with the following objectives:[35]

- Online consultations, using iPath, for subspecialty sign-out
- Online support to improve histologic/cytologic techniques
- Online case discussion and lectures
- Support for preparation of publications

Finally in 2010, phase one of the Pan African e-Network went live in 29 African countries.[16]

Telepathology in South Africa

Computers with various applications, some of them specifically designed to support laboratory operations, we increasingly introduced into many pathology laboratories around South Africa. For example, in the pathology laboratory of Mthatha General Hospital, these computers were originally supplied by the University of Transkei (now re-named Walter Sisulu University). This allowed pathologists to develop a database using the DataEase software package, which allowed for limited statistical computations to take place. These statistics were used for cancer registries and research. The first computers networked to the Internet were installed at Mthatha General Hospital's pathology laboratory by the health systems trust project (funded by the Henry J. Keyser Foundation, USA) in 1995. These computers – connected to the Internet via analog modems over ordinary telephone lines with the central dial-in node set in Durban, South Africa – were primarily used for sending and receiving E-mail. E-mail attachments were used to transmit histology images and pathology reports (both anatomic and clinical). Health workers from rural hospitals and clinics around this region of South Africa were able to thereby receive their lab results via E-mail. This dial-up system would see enthusiastic uptake and active use until 1998, at which point it was replaced by a web-based information site with online discussion groups (http://www.healthlink.org.za/).

Later in 1995, these computers – now with dedicated modem-based links between the Department of Pathology of the University of Transkei and the Department of Anatomic Pathology of the Medical University of Southern Africa – were used to send still images (microscopy, X-rays, computed tomography (CTs), ultrasounds) to the Telepathology Services of the Armed Forces Institute of Pathology (AFIP) in Washington DC, USA, via the Internet. At first, only static photomicrographs were sent; later, radiology and dermatology images were sent along with the photomicrographs [Figure 1]. Initially, all files were compressed for send-out using the program ISSA (Med Tech, Zagreb), which was installed at both Mthatha General Hospital and the AFIP. Later on, the AFIP introduced a more user-friendly web-based online attachment system for further ease of use. It should be noted that all cameras used in this project at this time were analog and as such scanning/digitization was

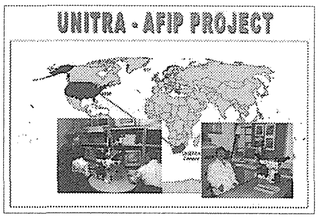

Figure 1: The telepathology project between the Armed Forces Institute of Pathology (left) and Mthatha General Hospital (right)

necessary as an intermediate step before the images were sent along to the AFIP. This project would eventually extend into a larger initiative to connect smaller remote hospitals in South Africa and to similarly provide them with remote pathology, cytology, and hematology consultation.[2,36]

The National Committee on Telemedicine and Tele-education was formed in 1998; this committee developed a National Telemedicine Strategic Plan that included several telepathology projects under its umbrella. Phase I of the National Telemedicine Strategic Plan was implemented between March 1999 and September 2000, establishing 28 telemedicine sites in six of the nine provinces of South Africa. Modem-based connectivity was replaced with ISDN (256 kbps) lines, which provided sufficient bandwidth for real-time video conferencing, teleradiology, and telepathology [Figure 2]. Unfortunately, because there was initially relatively low usage of this telemedicine system by pathologists, the software packages used were optimized for teleradiology, not telepathology. As such, the telepathology portions of this system would later migrate to the iPath platform (see section: Data Management Platforms).[14,37,38]

In 1999, a teledermatology project was initiated in Port St. Johns, South Africa, with the aim of improving access to dermatologic care for patients and for the education of family practitioners. In 2002, this project also migrated to the iPath platform. By 2003, this project was connected to a telemedicine network run by the Telemedicine Unit of the University of Transkei in Umtata.[17]

In 2001, as part of an e-health learning initiative, the Free State Department of Health in South Africa set up an interactive satellite broadcasting system that was offered to 40 health and training venues. This initiative extensively utilized iPath for telepathology purposes – with a link between Switzerland, South Africa, and other developing countries – and achieved over 18,000 consultations over the next 4 years. Discussion groups included topics about HIV/AIDS treatment, renal pathology, dermatology, and other topics. This system – which is still in operation today – is now also used to support problem-based e-learning for the medical students at Walter Sisulu University by digitizing exhibits (X-rays, lab results, etc.) and presenting them online.[13,14] 2001 is also significant as it was the year that the National Health Laboratory Service (NHLS) was formed in South Africa, with the purpose of incorporating and electronically connecting all the state laboratories around the country (http://www.nhls.ac.za/). All results from these laboratories are now computerized, stored in a central system, and made electronically available to practitioners around the country.[39]

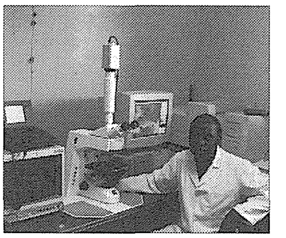

Figure 2: The South African Telemedicine System at St. Elizabeth Hospital, Lusikisiki

A mobile pathology laboratory was designed by the South African national Defence Force in 2004, equipped with a remote-controlled Zeiss microscope that could be manipulated via satellite or landline. Operation of this Zeiss microscope is still supported by a dedicated technologist.[40] By 2008, three Nikon Coolscopes had been installed in NHLS laboratories in the cities Mthatha, East London, and Port Elisabeth and connected via local area network (LAN), allowing remote control of the microscopes from any personal computer (PC) on the NHLS network. These laboratories are run by a small number of pathologists, without access to full immunohistochemical studies for some surgical pathology cases, which occasionally makes final diagnosis difficult. This system of Coolscopes is mostly supported by the pathologists located at Stellenbosch University in Cape Town – where it is mostly employed for dermatopathology and oral pathology cases. In 2008, a Zeiss Mirax WSI scanner was installed at the NHLS branch of Mthatha, which is currently utilized primarily for teaching purposes.[39]

Data Management Platforms

A clinical and research database was used in 1997 to standardize HIV studies in South Africa. This database utilized the systematized nomenclature of medicine (SNOMED) as its coding system and had both client-server and wide area network (WAN) mappings. This system is significant for being the first medical data management system reported in the African medical literature.[41] The implementation and widespread success of iPath servers in Africa, as described in section: Telepathology (Africa) above, provided a powerful platform to manage pathology data in Africa for several reasons:

- Ease of use
- Built atop a LAMP stack using standard, open-source technologies
- Inexpensive (essentially provided for free)
- Minimal hardware requirements

Unlike other areas of the world such as the USA where computing hardware and software is relatively cheap and ubiquitous, in Africa these resources are comparatively scarce (limited vendors) and more expensive. Hence, in this kind of environment, software platforms that are free and that can run efficiently on older hardware – iPath being one example – can flourish. As such, open source software has made significant inroads in Africa; this trend is likely to continue in the future.[42]

Laboratory Information Systems (LISs)

As section: Telepathology in South Africa indicates, in South Africa, all pathology reports from the NHLS are managed and stored in a central system.[39] Several international data management companies (e.g., Afrosoft International, MEDITECH) also market pathology-centric software packages (e.g., Afrosoft VeriLIMS, MEDITECH LIS) in South Africa.

Many of the LIS installations in sub-Saharan African countries are international projects (usually executed with the help of international non-governmental organizations such as Baobab Health), and are mainly focused on tracking, diagnosing, and defeating common infectious diseases (e.g., AIDS, malaria). This is the case for the Pan-African e-Network,[16] and for collaboration between the University of North Carolina at Chapel Hill and the Malawi Ministry of Health to install a LIS in Malawi.

In many West African countries, pathology services are usually limited to major academic centers and tertiary care hospitals, and LISs are not usually available. Consequently, most pathology reports are still totally paper-based.[43]

Teaching and Continuing Medical Education (CME)

Medical informatics has been included as a standard part of the undergraduate medical education program in South Africa since 1984.[44] It has kept abreast of technologic innovations, utilizing resources from the country's nationwide telemedicine project and technologies such as WSI scanners as they have become available.[39] In recent years, for instance, telepathology platforms like iPath have been used to facilitate problem-based learning at the University of Transkei/Walter Sisulu University.[35,45] Since 1992, an annual health informatics workshop for various categories of healthcare providers has been held by the Teaching Hospitals Complex and the Computer Sciences Department of Obafemi Awolowo University in Nigeria. This workshop has been a great success, with attendance increasing each year. Workshops like this have been proposed as a model for health informatics training in low-resource countries.[46]

A study at the University of Natal Medical School in South Africa was published in 1996. This study divided students in a histology course into two groups: One was given access to a computer aided instruction package along with standard microscopic learning, and the other was not. Members of the former group spent less time in the regular microscopy lab and showed a slight greater improvement in knowledge relative to students in the latter group.[47] Africa Calls is an annual series of audio teleconferences established by Dr. David Kaminsky in the USA, after he visited South Africa in 1997, with the support of the Annenberg Center for Health Sciences. Since 1999, audio teleconferences broadcast to centers in Botswana, Ghana, Namibia, Nigeria, South Africa, Sudan, Swaziland, Tanzania, Uganda, and Zimbabwe have formed the basis for customized educational programs in cytopathology, including informatics. These programs have been supplemented with downloadable learning material (e.g., PowerPoint slide decks) and other relevant educational material.[2,48] Finally, the first histopathology course in the history of Bulawayo, Zimbabwe was implemented in 2009. This course utilized materials from the local hospital libraries, the Internet, and local clinicians. Response to the inaugural course was enthusiastic, and the course gains more participants every year it is offered.[49]

Image Analysis

Image analysis papers that stem from Africa are rare. Only a single example could be found. In 1994, the Institut Pasteur de Madagascar in Antananarivo, Madagascar, studied the *in-situ* cellular immune response and associated fibrosis in mucocutaneous leishmaniasis due to *Leishmania braziliensis* utilizing automatic image analytic methods.[50]

THE AMERICAS

Canada and The United States of America

Canada

University and Government Infrastructure

The first few decades of pathology informatics in Canada were dominated by three influential National Health Informatics Organizations. The oldest of these is the Canadian Organization for the Advancement of Computers in Health (COACH). This member-supported organization was founded in 1975 and currently boasts over 1,500 members. As its name suggests, COACH has primarily focused on the use of computer technology in healthcare as well as the effective use of health information for decision-making. COACH holds national conferences and offers a professional certification in health informatics.[51] The second historically significant Canadian organization is the Canadian Institute for Health Information (CIHI). CIHI was founded in 1994 by federal, provincial and territorial governments as a not-for-profit corporation with a mandate that included setting national standards for health information technology and collecting, processing, and maintaining

health related databases and registries.[52] The third organization, Canada Health Infoway, is a federally funded corporation created by the Premiers of Canada's provinces in 2001. Since its creation, this organization has been a primary driver of health informatics in Canada, providing partial funding for numerous informatics related initiatives. Although the primary goal of the Canada Health Infoway is to accelerate the development of electronic health records (EHR) across Canada, five of the 193 projects it has funded up to 2011 have focused on LISs.[53] Additionally, the Alberta Netcare portal represents a significant milestone in Canadian pathology informatics. Created in 2003, Netcare is a repository for essentially all laboratory data generated in the province of Alberta as well as for radiology, clinic notes, allergies and medication information. A secure login is available to healthcare providers in the province.[54] More recently, the province of Saskatchewan implemented a similar database, called the eHealth Portal.[55] In the province of British Columbia patients can directly access their own laboratory test results through a secure website called MyeHealth.[56] The province of Alberta has a similar website, part of their myHealth web service, in the planning stages.[57]

LISs

Despite the influence of these organizations, many laboratories in Canada were slow to adopt LISs. The first generation systems began to appear in Canadian hospitals in the 1980's, but some anatomic pathology services in smaller communities still relied on type writers and carbon paper as late as 2005. With the exception of a large home-grown LIS in Ontario, Canadian Laboratories have tended to adopt the best North American LIS. Meditech has installations in a number of provinces including British Columbia, Alberta, Ontario and Nova Scotia and is particularly popular in rural and community hospital settings. Cerner has LIS installations in several major Canadian population centers and academic teaching centers as does Sunquest. Sysmex has a large installation in the province of Manitoba. Like the United States, analyzer-LIS interfaces are a mixture of homegrown solutions and vender-supplies middleware. However, increasingly laboratories are moving toward commercial/vender-supplied software to fill this need. Overall, the relatively slow uptake of computer technology in Canadian laboratories may be seen as a reflection of the generally slow adoption of computer technology by Canadian physicians in general. Even in 2012, many primary care physician offices do not use computers at all, much less electronic medical records.

In recent years, there has been an interest in enhancing the functionality of LIS systems to support additional operational and research objectives. A major area of interest in this regard is synoptic reporting for anatomic pathology. In 2012, the non-profit group Canadian Partnership against Cancer with the support of the Canadian Association of Pathologists launched an initiative to implement synoptic reporting across Canada by 2017.[58]

The second area of interest is in using the LIS to assist in utilization management of laboratory tests Predictably, in light of its publically funded health care system, Canada has a long history of interest in utilization management, dating back to 1965.[59] Historically, interest in using the LIS to aid in utilization management has been centered at the University of Ottawa,[60-62] and the University of Edmonton[63] as well as other centers.[64,65] In 2013, the Alberta government established a provincial laboratory utilization office with the intent of using LIS systems in the province to support utilization management initiatives.

Education and Training Opportunities

In academic circles, it is only in the past several years that pathology informatics has begun to have a voice in Canada independent of health informatics in general. In July 2009, the Canadian Association of Pathologists added a Special Interest Group in Pathology Informatics. This group has been chaired alternately by Dr. C. Naugler from the University of Calgary and Dr. G. Yousef from the University of Toronto. This group presents a series of short talks each year at the Canadian Association of Pathologists Annual Scientific Meeting. In 2010, the University of Calgary became the first Canadian Institution to offer an official pathology informatics training experience opportunity when it launched a 1 month pathology informatics elective open to laboratory medicine residents. In 2011, the University of Toronto launched a virtual rotation in pathology informatics for the anatomical pathology residents. Currently, academic pathology informatics is centered in three Canadian university departments (Dalhousie University, University of Toronto and the University of Calgary), all of which have academic pathology informatics faculty. However, as of 2013, there are no pathology informatics fellowships available in Canada. A number of other universities have very strong research and teaching programs in bioinformatics including the University of British Columbia and Dalhousie University.

Telepathology

The geography of Canada with cities separated by vast distances suggests that telepathology may have a particularly promising future in this country. Despite this, Canada has been relatively slow to embrace telepathology, with the University Health Network in Toronto establishing the first operational system in 2010. This system links several remote northern hospitals to subspecialist pathology support at University Health Network hospitals.[66] It is likely that this model will be repeated in a number of geographically isolated regions in the coming years. Indeed, the necessary infrastructure is gradually accumulating, with whole slide imagers now in routine use for teaching at a number of academic pathology departments. In hematopathology, several large scale installations of the CellaVision system are in use in Nova Scotia, Ontario and Alberta.

In 2011, General electric (GE) Healthcare opened its Pathology Innovation Centre of Excellence as part of the Toronto MaRS Discovery District of technology companies. The facility includes a digital laboratory to facilitate training, research and development on the Omnyx Integrated Digital Pathology platform.

The United States of America

This history of pathology informatics – especially in the USA – resembles a train station from which multiple tracks have emerged and intermittently crossed paths. Historical events are presented chronologically in Figure 3. However, for ease of reading, the history of each area of study within pathology informatics is discussed separately where possible, allowing for the fact that some of these categories have overlap.

1950s	1960s	1970s	1980s	1990s	2000s	2010s
1952: First computers used in clinical labs.	**1962:** CAP establishes the first computer education program for pathologists. **1964:** LINC system described in JAMA. **1965:** Systematized Nomenclature of Pathology published **1968:** National Committee for Clinical Laboratory Standards (NCCLS) founded. First system for remote pathologic diagnosis demonstrated.	**1970s:** LISs in standard use in clinical labs. **1976:** SNOMED first edition published. First online surgical pathology system in the USA becomes operational at the Massachusetts General Hospital. **1977:** American Blood Commission's Committee for Commonality in Blood Banking Automation recommends adoption of ABC Codabar for blood product labels. **1979:** First regularly scheduled national seminar in pathology informatics (ASCP, twice per year, 1979-1986).	**1980:** First paper describing rotations in pathology informatics for residents is published. **Early 1980s:** First NLM sponsored informatics fellowships are made available. **1983:** First AIMCL meeting. **1984:** *Informatics in Pathology* journal launched. Laboratory Information Systems Division of the AACC formed. **1985:** FDA mandates use of ABC Codabar on all US blood products. **1986:** First telepathology publication. UMLS project begun at the NLM. First calls for pathologists as medical information specialists. **1987:** HL7 is founded with subsequent formation of Laboratory and Anatomic Pathology working groups. **1989:** First book on pathology informatics published.	**1990:** Medical informatics is defined as a medical subspecialty in *JAMA*. **1992:** American Board of Pathology proposes a specialty in informatics to the American Board of Medical Specialties. **1994:** LOINC project is initiated. **1996:** First virtual microscope system developed. First APIII meeting held. NCCLS creates the Area Committee on Automation for creation of standards in laboratory automation including barcoding. **1997:** IHE is formed with subsequent formation of Laboratory and Anatomic Pathology groups. **1998:** ISBT 128 international barcoding standard approved for labeling human transfusion and tissue products.	**2000:** First pathology informatics organization is chartered (API). **2003:** First FDA clearance for quantitative image analysis of immunohistochemical cancer markers. HL7 creates a Genomics Working Group. **2004:** First LabInfoTech Summit. CAP Foundation creates mini-fellowships for pathology informatics. **2005:** Working Group 26 for Pathology is created in DICOM. NCCLS changes its name to CLSI. **2009:** Digital Pathology Association is formed.	**2010:** *Journal of Pathology Informatics* is launched. First combined (APIII + LabInfoTech Summit) Pathology Informatics meeting. **2011:** Clinical informatics becomes official ABMS subspecialty. First nationwide retreat for pathology informatics fellows held in Boston, MA.

Figure 3: Major events in the history of pathology informatics in the USA

Pathology Informatics as a Term and a Medical Subspecialty

Informatics, including pathology informatics, in the USA began in the early 1950's. The word "Informatik" was first coined in a German publication and likely arose from a combination of "information" and the suffix "-atics," which is derived from Greek and means "the science of".[67] This was shortly followed by use of "informatique" by the French, "informatika" (информатика) by the Russians, and finally "informatics" in English-speaking countries including the USA.[67-70] Subsequently, the first definitions of medical informatics as a clinical and research medical subspecialty appeared in the Journal of the American Medical Association (JAMA).[71]

During the same year that clinical informatics was introduced to the medical literature (1990), Dr. Bruce

Friedman is first credited with using the term "pathology informatics" while concomitantly advocating for the development of separate divisions of pathology informatics within pathology departments. He described the key benefits of having such a division, which included: (i) enhanced productivity and efficiency in application development, (ii) better management of pathology information with oversight by informaticists (also called informaticians), (iii) increased departmental political power, and (iv) increased awareness and sophistication among departmental leaders in information technology.[72] These advantages continue to be true today. Informatics as a recognized subspecialty within pathology was further championed by others who declared that pathology informaticists should play a key role in defining, selecting and implementing all information systems in a pathology department, in addition to being involved in information systems planning for a healthcare enterprise.[73]

Recognition of informatics as a bona fide academic medical subspecialty lagged behind actual practice of informatics (information management) for a time, despite the above efforts. Lack of reimbursement for clinical informatics service likely contributed to limited publication options and research funding as well as recognition from peers.[74] Similarly, clinical wards, outpatient offices and clinics still relied heavily, if not entirely, on paper records, including printouts of laboratory results and reports. This was probably related, in part, to the fact that hospitals were spending an average of only 2% of their budget on information systems.[75] However, as federal legislation surrounding cost accounting, delivery of healthcare and quality laboratory practices began to increase in the late 1980s, including but not limited to the Clinical Laboratory Improvements Act of 1988,[76] more attention was paid to the use of computer systems in healthcare as a whole. Compounded by the promulgation of PCs with graphical user interfaces and the advent of interfaced communications (vide infra), the use of computers in the hospital setting began to skyrocket. As human-computer interactions in medicine began a sharp ascent, the need for physicians to act as medical information specialists (informaticists) was more widely accepted.[71,75,77]

In 1992, the American Board of Pathology (ABP) sent a letter of intent to create an informatics subspecialty to the American Board of Medical Specialties (ABMS). Subsequently, a five-member informatics test committee was convened to write questions for the examination. This effort was unsuccessful at that time for two reasons. Much of informatics involves medical knowledge and complex managerial skills which are difficult to adequately represent in written questions with multiple choice answers, and questions on technical topics were considered insufficient for a clinical informatics board exam.[78] However, beginning in 2009, renewed interest in a board-certifiable subspecialty in clinical informatics spurred the publication of several papers describing criteria for a fellowship in clinical informatics in the Journal of the American Medical Informatics Association.[79-81] In September of 2011, the ABMS announced its approval of clinical informatics as a board-certifiable medial subspecialty. The application was brought forth by the American Board of Preventive Medicine with co-sponsorship by the ABP. This board examination breaks new ground because, unlike most other board examinations which are only open to a few medical specialties, any qualified candidate with primary certification in any ABMS primary specialty may sit for the clinical informatics board examination. Currently, the first examination is anticipated to take place in the fall of 2013. This will hopefully spawn more fellowships in clinical informatics that accredited by the American Council on Graduate Medical Education. At present, however, practicing pathologists may still sit for this board exam under the by-experience pathway, at least for the first five years that the board examination is available.

Use of Computers in Laboratories

Shortly after informatics was defined as a term in the early 1950's, the earliest evidence of data processing in the medical laboratory was reported. Dr. Arthur E. Rappoport presented his experience with the "McBee manual punch card for laboratory data" at the 1952 meeting of the American Society for Clinical Pathology (ASCP).[70] During the next decade, a number of events took place which demonstrated the need for information technology in the laboratory space. At the 1962 meeting of the ASCP, Dr. Rappoport demonstrated the use of IBM punch card systems in the laboratory.[70] In 1964, JAMA published the first article describing a laboratory computer system. This system, called the Laboratory Instrument Computer, was developed by the Massachusetts Institute of Technology.[82,83] Several other early publications in the field, including a monograph, were contributed by Dr. Donald Lindberg.[84-87]

By the 1970's, computer systems were in widespread use in clinical laboratories.[74] Figure 4 illustrates the Spear CLAS-300, an early LIS from circa 1971. The first commercially supported LIS, from a vendor which still today provides such laboratory systems, was implemented at Cape Cod Hospital in 1972 by Meditech. The quantitative nature (i.e., numerical data) of clinical laboratory results and the necessity of performing repetitive calculations helped incentivize laboratories to computerize their processes. These aspects of clinical laboratory data also facilitated automation more quickly than in anatomic pathology laboratories and other areas of healthcare. The first laboratory audio response system – DIVOTS – was developed by Dr. Rappoport at the Youngstown Hospital Association in 1975. CAPER,

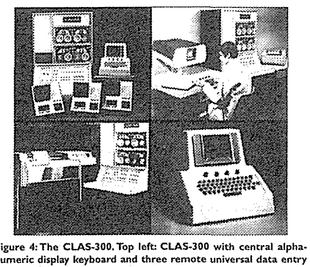

Figure 4: The CLAS-300. Top left: CLAS-300 with central alphanumeric display keyboard and three remote universal data entry terminals. Top right: data entry on the CLAS-300 (note the large size of the computer components, as well as the magnetic tape-based storage). Bottom left: the CLAS-300's line printer; this particular model, which featured a speed of 300 lines per minute, was considered an incredibly fast printer by 1970's standards. Bottom right: the CLAS-300's central input station; though a large *unit, this station was – like the smaller remote data entry terminals:* A "dumb" terminal that merely reflected the state of the mainframe that powered it. Photographs reproduced with permission

the first online surgical pathology information system was implemented in 1976 and served as the inspiration for successive generations of anatomical pathology systems, including Surepath (1978, Tufts), and in 1983 CoPath (descendants of CoPath remain market leaders today). Likewise, the structured textual data used in microbiology proved challenging to implement, but the model created by Peebles and Ryan in 1979 continues to be a crucial component of the Sunquest LIS. Until the late 1980's, information technology in laboratories and other ancillary care areas such as the pharmacy and radiology continued to progress, but most hospital information systems (HIS) were focused on capturing charges rather than the delivery of patient care.[73,77] By contrast, automation, with its concomitant reduction in cost per test, furthered the laboratory's strength as a revenue center for the hospital.[74,75]

Automated Capture and Exchange of Laboratory Data

Laboratories enabled with computer technology quickly realized the need to automate transfer of data from the specimen to the instrument to the LIS, and later to the EHR. One of the first aspects of such automated data transfer was realized in the use of barcodes. Concomitantly with the birth of the term informatics and the use of computers in the laboratory, Bernard Silver and Joseph Woodland of Drexel University were granted the first barcoding technology patent in 1952. Adoption of barcodes was initially slow. While the first use of early barcodes in the commercial setting was in 1966, widespread use did not become reality until the mid-1970s.[88] Again, laboratories seemed to be ahead of their medical counterparts in the adoption of new technologies into healthcare. Dr. Arthur Rappoport implemented many creative uses of barcodes in his laboratory in the 1960's and 1970's. While many clinical applications did not utilize barcodes until the 1990s, transfusion medicine made far earlier calls for the use of barcodes for transfused products. In 1977, The American Blood Commission's Committee for Commonality in Blood Banking Automation recommended the adoption of Codabar barcodes for blood product labels. The use of Codabar on blood products was mandated by the United States Food and Drug Administration (FDA) in 1985. In 1994, a new barcode system based on Code 128 symbology was approved by the International Society for Blood Transfusion called ISBT 128.[89] ISBT 128 has been very slowly adopted over the last 17 years as transfusion laboratories are only just now being required to comply with this new standard. By the early 1980's, many laboratory instruments accepted barcode-labeled specimen tubes, and laboratories took advantage of this capability for more rapid, accurate specimen identification as well as automation.

Exchange of data over network lines came later. Health Level 7 (HL7) was formed in 1987 to provide standards for communication of health information between different systems, thereby improving the efficiency of interface implementation and accuracy of data transfer. The formation of several working groups including laboratory, anatomic pathology and genomics took place in the years that followed. In 1997, an organization called Integrating the Healthcare Enterprise (IHE) was formed with subsequent formation of laboratory and anatomic pathology working groups. The overall goal of IHE is to promote the coordinated use of established standards such as HL7 to address specific clinical needs in support of optimal patient care. Just prior to this in 1996, recognition of the importance of automation in *the clinical setting increased as the National Committee* for Clinical Laboratory Standards (NCCLS) formed an Area Committee on Automation to provide additional technical standards for all aspects of laboratory automated data exchange and workflow including barcoding, interface implementation and robotic lines that move specimens between different instruments for testing.[90-92] In 2005, the NCCLS changed its name to the Clinical and Laboratory Standards Institute (CLSI), to which it is now referred.

Additional discoveries by pathology informaticists furthered automation in several areas. Development of a single system to electronically collect, analyze and manage point-of-care testing data across devices from multiple vendors can be attributed to pathology informatics,[93] and pathology informatics often still leads the way in the implementation of Lean, six sigma, and automation systems for laboratories,

resulting in workflow efficiencies and improvements in patient safety.[94-97] Similarly, automated reporting of critical laboratory values with streamlined tracking of communication hand-offs have been generated through the work of pathology informatics.[98]

Ontologies, Terminologies and Coding Systems

Shortly after the advent of computer technology in the laboratory, the College of American Pathologists (CAP) recognized the need to define an ontology surrounding pathology concepts. The systematized nomenclature of pathology (SNOP) was published by the CAP Committee on Nomenclature and Classification under the direction of Dr. Arthur Walls in 1965. Under the long-term leadership of Dr. Roger Cote, SNOP evolved into the SNOMED. The first edition of SNOMED was published in 1976, the 2nd edition in 1979, 3rd (international) edition in 1998, Reference Terminology in 2002 (when Dr. Kent Spackman took up the baton), then following a merger with the British nomenclature Read codes, SNOMED-Clinical Terminology was published in 2004. The CAP with perfect foresight funded and supported the development of SNOMED for almost 30 years. Since then, SNOMED has transitioned to a truly international code, now co-sponsored and funded by 18 countries. It is now owned and licensed by the International Health Terminology Standards Development Organization.[99] It is anticipated that the international classification of diseases, 11th revision will be based on SNOMED. It is rewarding to witness how a pathology-inspired terminology initiative has become the world-wide standard for standardized and structured medical terminology.

SNOMED-CT today is the most comprehensive, multilingual clinical healthcare terminology in the world. Dr. Donald Lindberg, a pathologist and informaticist who has been the long-term head of the National Library of Medicine (NLM) started another terminology project called the unified medical language system in 1986 to facilitate the creation of more effective and interoperable biomedical information systems and services, including EHRs.[100] As the availability of automated data exchange grew, so did the scope of that exchange. Laboratories that once only used such technology for transfer of data between the test instrument and the LIS began to expand into the transfer of data between different laboratories. They quickly realized that gaps in the HL7 standard led to challenges associated with transferring test results for the same analyte, but with different methods and reference ranges. Rather than, continue with dependence on idiosyncratic test codes developed in each laboratory independently, the Regenstrief Institute at Indiana University, in cooperation with laboratorians from Utah and the USA and Canada developed a standard coding system for tests and their methods called logical observation identifiers names and codes (LOINC) in 1994.[101] LOINC facilitates the exchange and pooling of results for clinical care, outcomes management, and research and may be used in conjunction with HL7 to ensure correct mapping of test results within a database. Current draft proposals for the Health Insurance Portability and Accountability Act[102] electronic claim attachment standards are based on LOINC codes.[103] Also, the ability to send and receive laboratory results encoded with LOINC codes are an important part of the meaningful use regulations now being implemented by the US Office of the National Coordinator for Health Information Technology.

LIS Vendors

The use of LISs in USA laboratories has depended almost entirely on supply of such software by commercial vendors who install and support these systems. There have been isolated instances of home-grown/self-developed software being used in hospital laboratories, but there have been probably fewer than two dozen long-term survivors. On the other hand, long-term installations of vendor-supported systems have numbered in the thousands.

The history of the LIS is replete with many instances of vendors either going out of business or being absorbed or acquired by other entities. Interestingly, it has been the larger, non-laboratory specific companies that have had the shortest "lifetimes" as LIS providers. Examples include General Electric, International Business Machines, Digital Equipment Corporation, Honeywell, Beckman, Technicon, and Control Data Corporation among others. In contrast, the smaller, laboratory-dedicated firms experienced longer lifetimes, and although often acquired, their LISs were usually continued in use. The USA firm with the longest longevity in the LIS domain is Meditech who installed its first LIS in 1972, and is today still one of the market dominant vendors. Other firms with long, continuous histories as LIS providers include Mckesson, Sunquest (Misys), Cerner (PGI), Computer Programs and Systems Incorporated, Diamond Computing, Comp Pro Med, Psyche (SAC), and Soft Computer Consultants. Of 64 LIS firms in business in 1988, only 15 remain in business today. Over the years, despite competition for a dwindling number of potential customers, new firms have entered the market. As of 2011, 33 companies offer complete LIS solutions. Figure 5 offers a reasonably complete timeline of LIS vendors serving the US market from the late 1960's to the present.

Digital Pathology, Telepathology and Image Analysis

The use of digital images in pathology was a latecomer to the pathology informatics scene. In 1968, analog video-based telepathology was first demonstrated by Ronald Weinstein and colleagues in Boston via a link between Logan International Airport and MGH [Figures 6 and 7]. This showcased the potential

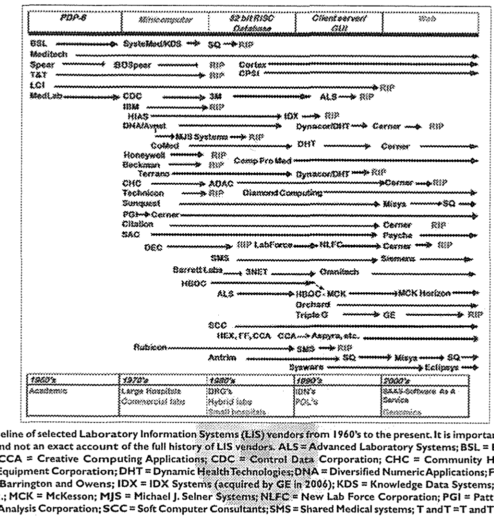

Figure 5: A timeline of selected Laboratory Information Systems (LIS) vendors from 1960's to the present. It is important to note that this is a sampling and not an exact account of the full history of LIS vendors. ALS = Advanced Laboratory Systems; BSL = Berkeley Scientific Laboratories; CCA = Creative Computing Applications; CDC = Control Data Corporation; CHC = Community Health Computing; DEC = Digital Equipment Corporation; DHT = Dynamic Health Technologies; DNA = Diversified Numeric Applications; FF = Fletcher-Flora; HBOC = Huff, Barrington and Owens; IDX = IDX Systems (acquired by GE in 2006); KDS = Knowledge Data Systems; LCI = Laboratory Consulting, Inc.; MCK = McKesson; MJS = Michael J. Selner Systems; NLFC = New Lab Force Corporation; PGI = Patterson, Gorup, Illig; SAC = System Analysis Corporation; SCC = Soft Computer Consultants; SMS = Shared Medical systems; T and T = T and T Technology (Peter Tong). Image courtesy Weiner Consulting Services and Dennis Winsten and Associates

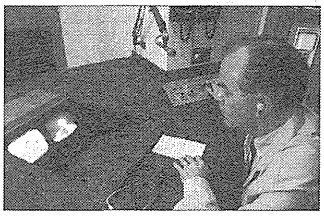

Figure 6: The live telepathology system connecting Boston Logan Airport and the Massachusetts general hospital in action. This is widely considered the first working telepathology system in history

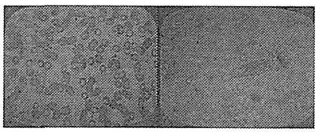

Figure 7: Examples of the video streams the first telepathology system could generate. Left: peripheral blood smear; right: Urine cytology

for image-based pathology informatics to have a positive effect on the practice of surgical pathology, cytopathology and hematology. With the advent of increasingly affordable digital imaging technologies, such early analog efforts paved the way for the emergence of digital pathology. The first publication describing the use of dynamic robotic telepathology occurred in 1986 [Figure 8], and an early publication describing a "virtual microscope" prototype which included the concept of WSI was published 10 years later. This publication forecast correctly that digital slides would not only conveniently emulate a physical microscope for clinical interpretations and teaching,

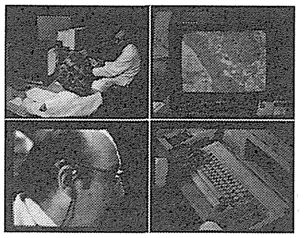

Figure 8: Live demonstration (in 1986) of the first operational robotic telemicroscopy system in history. Top left: Dr. Alexander Miller and associate operating the robotic telemicroscopy system; top right: example of the video feed from the system; bottom left: Close-up of videoconferencing gear worn by participants; bottom right: Close-up demonstrating keyboard control of remote robotic microscope

but also that digital images would be used to better screen and characterize malignancies, generate three-dimensional (3D) reconstructions, and permit image analysis using various special stains that revealed the presence or absence of biochemical markers.[104,105] Over the ensuing years the field of digital pathology continued to evolve with faster and better whole slide scanning technologies and computational algorithms to analyze the images. The first national course on digital pathology led by Mariano Alvira, Peter Shireman and John Minarcik was presented by the ASCP both at its national meetings and at its Chicago headquarters beginning in the early 1990's. Early efforts in image analysis can also be attributed to researchers in pathology informatics.[106,107] Automated slide scanners with image analysis algorithms on board were designed to screen cervical cytology smears for abnormal cells. Such instruments first began to receive clearance for clinical use by the FDA in 1995.[108] FDA clearance for image analysis algorithms enabling quantitative analysis of immunohistochemical cancer markers for estrogen receptor, progesterone receptor and others first occurred in 2003.[109] Research continues with extensions into parallel and grid-based systems capable of supporting digital slide sign out in routine surgical pathology practice, computer-aided diagnosis, content-based image retrieval, and 3D image reconstruction.[104,110-112] As the use of WSI evolved, the need for imaging standards specific to pathology emerged. The Digital Imaging and Communications in Medicine (DICOM) standard was initially developed to house radiological images, but in 2005, the Working Group 26 (Pathology) was added to specifically incorporate WSI into the specification. Since that time, Working Group 26 has published two supplements to the DICOM standard.[113,114]

Education Efforts in Pathology Informatics

Approximately 10 years after the first reports of computer use in a laboratory, the CAP established the first computer course for pathologists at their annual meeting.[99] In 1979, the ASCP began offering the first regularly scheduled course in pathology informatics entitled "The ABCs of LIS." This was offered at every ASCP national meeting, fall and spring, from 1979-1986. Fellowships in medical informatics (this was general informatics – not pathology informatics) began to appear in the early 1980's, funded by the NLM and again spearheaded by Dr. Donald Lindberg.[115] In 1986, the first journal article, which called for pathologists to be medical information specialists appeared in the literature.[116] The first pathology informatics book, called "The ABCs of LIS", was published by Dr. Frank Elevitch and Dr. Ray Aller (based on their ASCP course) in 1986, with a revised edition published in 1989,[117] In 1980, the first article was published on training pathology residents in informatics,[118]. but subsequent articles did not appear until a decade later. In 1984, Dr. Frank Elevitch was appointed Chair of the CAP Lab Computer Committee (LCC), subsequently termed the Informatics Committee and more recently the Diagnostic Intelligence and Health Information Technology Committee. Under his leadership, the members of the LCC proposed, prepared, and presented an enormous number of CAP national meeting seminars on pathology informatics. Indeed, for much of the ensuing decade, more than 50% of the courses at the CAP National Meeting were focused on informatics. Although this strengthened informatics expertise at many community practices, academic centers did not appoint sufficient faculty, or permit them sufficient focus, to strengthen residency training. Because of ongoing gaps in pathology informatics expertise at many residency training programs at that time, the CAP began to develop several informatics mini-fellowships in the late 1990's to early 2000's. In 1995, the first formal pathology informatics fellowship in the nation was established by Dr. Michael Becich at the University of Pittsburgh Medical Center.[119] Today there are many more training opportunities (http://www.pathologyinformatics.org/content/training-opportunities-pathology-informatics), but still not enough to meet the emerging demand for skilled informaticists.

Professional Activities for Pathology Informaticists

The first national foci of pathology informatics began with the CAP courses of Rappaport and others in the 60's and 70's, then the ASCP course series of Elevitch and Aller 1979-1986, followed by the CAP seminars from the mid-1980's to 2000. A large amount of focused information was presented at user groups of various LIS vendors, such as Meditech, Sunquest, Cerner, and

Kontron.

The first national pathology informatics conference in the USA took place in 1983 in Ann Arbor, Michigan, entitled Automated Information Management in the Clinical Laboratory (AIMCL). One year later, the American Association for Clinical Chemistry formed a division of the organization dedicated to LIS.[120] A journal called "Informatics in Pathology" was launched that same year, but was unfortunately discontinued 1 year later due to poor subscription and insufficient contributions.[78] In contrast, the AIMCL meeting was quite successful, taking place annually for 21 years. Beginning in 1996, a second conference known as advancing pathology informatics, imaging and the internet (APIII), later renamed Advancing Practice, Instruction and Innovation through Informatics (still APIII), began to be held each fall, usually in Pittsburgh, Pennsylvania. While the theme of AIMCL tended to be weighted toward clinical pathology, APIII was initially more focused on anatomic pathology and digital imaging. The driving forces behind each of these conferences were Dr. Bruce Friedman and Dr. Michael Becich, respectively. As a result of their efforts and those of many others, the first professional organization specifically oriented to pathology informatics called the Association of Pathology Informatics (API) was chartered in 2000. Since its inception, the API has been a driving force behind a number of conferences and activities for pathology informaticists (http://www.pathologyinformatics.org/).

In 2004, AIMCL was replaced by the Lab InfoTech Summit which was held annually in Las Vegas, Nevada from 2004-2009. During this time, several international meetings related to pathology informatics were held including the First World Congress on Pathology Informatics in Australia organized by Michael Legg, Ulysses Balis, and Vitali Sintchenko, and conferences in Europe hosted by the European Congress on Telepathology and International Congress on Virtual Microscopy. The Digital Pathology Association subsequently formed in 2009. Toward the end of 2010, both the APIII conference and the Lab InfoTech Summit combined, in concert with the Histology Image Analysis group, to produce a single pathology informatics mega-event in Boston, Massachusetts, named Pathology Informatics 2010. That same year, a new open-access journal entitled "Journal of Pathology Informatics" was launched under the editorship of Dr. Liron Pantanowitz and Dr. Anil Parwani.[121] Most recently, in August 2011, the first-ever nationwide retreat for pathology informatics fellows was organized by and held at the MGH in Boston, MA.

Mexico, South America, Central America, and the Caribbean

1958-1989

Telepathology

In 1974, static black-and-white images of tissues, peripheral blood and bone marrow smears were transmitted via satellite from a hospital ship docked in Brazil to Washington DC, USA. It was the first time that still images of microscopic slides were transmitted by satellite communication.[122] The same year, Dr. Moacyr Domingos Novelli from the University of São Paulo published a report on the SACI Project (Advanced System in Educational Communication), which broke new ground in the usage of satellite communication in telemedicine in Brazil.[123] In 1981, the same group described its experiences with rendering remote histopathologic diagnosis from analog images obtained with optical microscopes that were then digitized and finally transmitted via satellite communication.[124,125] In 1985, the Mexican Centre for Health Education by Television (CEMESATEL) began transmitting clinicopathologic conferences from the Hospital Infantil Federico Gómez to 18 remote Mexican health institutions via satellite.[126]

Data Management

Computer data analysis in pathology was first reported in the South American literature by Friedrich *et al.* in 1977; their report describes a postoperative staging system for vulvar carcinoma.[127] One year later, Novelli *et al.* published their work on computerized data analysis in oral pathology.[128] Novelli's group would, 4 years later, also report on their research on terminology coding and database management in surgical pathology.[129] In 1985, a group of pathologists and engineers developed an information system for pathology and reported their experiences.[130] The same year, a team of researchers from the Universidad Nacional Autónoma in Zargoza, Mexico described an information system for oral histopathology.[131]

Image Processing and Analysis

Throughout the 1980's, Brazil was a hotbed for microscopic image processing and analysis (mainly focusing on oral pathology) as evidenced by the creation of the Laboratory of Informatics Dedicated to Odontology at the University of São Paulo in 1980.[132] In 1987 in Cuba, the first computer-based morphometric studies were performed on atherosclerotic lesions of the aorta at the Higher Institute of Medical Science of La Habana. In these studies, data was gathered with a digitizer interfaced with a NEC 9801 personal microcomputer. These data were then processed on a GDR EC-1040 minicomputer using SPSS (a statistical software package).[133] In 1989, studies on computer-aided morphometric analysis were published by the Laboratory for Cell Biology and Pathology of the University of São Paulo.[134]

Teaching and CME

In 1958, the University of Santa Maria (Río Grande do Sul, Brazil) utilized closed-circuit television for undergraduate

pathology education.[135] This was considered a pioneering use of that technology in the worldwide literature at the time. In 1986, Dr. Fernando Augusto Soares of the Ribeirão Preto Medical School of the University of de São Paulo published practical recommendations for pathologists on the use of computers.[136]

1990-1999

Telepathology

In 1993, the Department of Pathology of the Hospital of Hermosillo, Mexico (Roberto de León Caballero, Jorge Platt Garcia, and Minor Cordero Bautista) participated in 63.5% of all cases processed by the Arizona International Telemedicine Network that year. This network utilized static telepathology methods to reach hospitals across the world. Even with the technological limitations (static telepathology only; relatively low-resolution images), an 88.3% absolute concordance between telepathologic diagnosis and glass slide diagnosis was seen – with an astonishing 96.5% concordance for clinically significant diagnoses.[36,137]

Brazil and Mexico were avid users of the AFIP's Telepathology Service between 1994 and 1999. This service – described in section: Telepathology in South Africa – utilized static telepathology only in that time period and recorded a telepathology-to-glass concordance rate similar to that of the Arizona International Telemedicine Network (73% absolute concordance; 97% concordance for clinically significant diagnoses). These early static telepathology experiences highlighted the need for increased technical expertise on the part of both the referring pathologist and the telepathology consultant and increased training in the selection of appropriate regions of interest on the part of the referring pathologist.[138,139]

In 1994, RESINTEL's TRANSPATH network – briefly described in section: Telepathology (Africa) – had operational telepathology sites in Martinique and Guadeloupe Island. Unfortunately, by 1998 this network had to be shut down due to lack of funding. The ultimate fate of these sites is not known, but they are thought to be currently non-operational.[7]

On October 11th, 1996, Dr. Sergio González (Department of Pathology, Hospital Clínico of the Pontificia Universidad Católica de Chile) reported on the usage of a telepathology station that connected his institution with the Hospital Dr. Sótero del Río, also in Chile. This study concluded that the 10 Mbps connections afforded by their network offered good image quality for online S-video transmission from microscopes using a Silicon Graphics workstation to digitize and compress video signal from a Sony DXC-C1 camera mounted on the Olympus BH-2 light microscope.[141,142]

South America experienced a wellspring of telepathology activity in 1997. That year, the "Europe-Latin America Telepathology Initiative" – a pilot telepathology exercise – was funded by the European Union, with the participation of the Netherlands and the Belgrano Public Hospital in Buenos Aires, Argentina. It employed ISDN technology for its network connectivity.[143] Also in 1997, the Hospital de Clínicas de Porto Alegre in Brazil conducted a comparison study on tele-consultation in cytopathology of serous effusions.[144] Finally for 1997, the Enlace Hispano Americano de Salud (EHAS) Project as created to offer low cost radio (HF and VHF) links, with solar energy systems, in rural areas and other areas in South America where conventional telephony was not available. For instance, in the province of Alto Amazonas, Peru, this allowed for sending and receiving of E-mails between healthcare providers – a first for that geographically isolated province.[141]

Telepathology in South America continued to be strongly developed in 1998 and 1999. A videoconference session on telepathology, using three ISDN telephone lines (384 Kbits/s), between Santiago de Chile and Buenos Aires took place in 1998, during a Congress organized by the Hospital de Clínicas de Buenos Aires.[145] In October of 1998, a telepathology workshop was organized in Peru, between Lima (Universidad Federico Villarreal) and Arequipa (Universidad San Agustín). Its subject matter included tele-consultations, Internet, as well as image capture and processing.[146] Finally, in 1999, the Universidad Nacional de Colombia (UNC) implemented a remotely-managed robotic microscope – a first for this region of the world.[147]

Data Management

There were two notable events in pathology data management in South/Central America and the Caribbean, both of which took place in 1995. The Mexican National Epidemiological Surveillance System (SINAVE) was created that year, including an information system for the histopathologic records of malignant neoplasia.[148] Meanwhile, in Cuba, SARCAP – an automated registry and control system for pathology – was developed by the pathology department of the Hospital "Dr. Luis Díaz Soto." It was initially designed as an information system for both autopsies and biopsies but has since then expanded into a national database for registry and coding clinical autopsies in Cuba.[149]

Image Processing and Analysis

An Argentinian group from the Medical School of the University of Buenos Aires published a digital pathology image processing study in 1990.[150] In the same timeframe, another Argentinian group studied the morphometric determination of AgNORs in breast carcinoma.[151] Also in 1990, Novelli *et al.* created software called IMAGELAB for image processing and analysis of microscopic images.[152] Though Novelli's group was the most prolific it was far from the only Brazilian effort in digital pathology image analysis at the time; there were also active research groups at the Evangelical Faculty of Medicine of Parana, Brazil and the Adolfo Lutz Institute, São Paulo, Brazil.[153,154] In 1993, The Institut Pasteur de Guyane, Hopital Jean Martial, Cayenne, French Guiana published a paper on the use of computer-aided image analysis in the study of inflammatory cells in skin lesions of chromomycosis.[155] Finally, in 1994, the Department of Biomedical Engineering of the Universidad Nacional de Asunción (Paraguay) began a full-blow research initiative on biomedical images and cancer pathology.[156]

Teaching and CME

In 1994, Infomed – a Cuban health telecommunication network that supports Internet connectivity and web editing – was brought online. It became a very popular resource for anatomic pathology in that country and still enjoys considerable activity today (http://www.sld.cu/sitios/scap/). The first Virtual Hispano-American Congress of Pathology (http://www.conganat.org/) took place in 1997, with the participation of Argentina, Brazil, Cuba, Dominican Republic, and Mexico.[157] Since then, there have been 10 further convocations of this virtual Internet congress. Dr. György Miklós Böhm, a Professor of the Department of Pathology, Faculty of Medicine, University of São Paulo, created the first Brazilian Telemedicine and Medical Research Laboratory in 1998.[158] Finally, a multinational virtual health library known as Biblioteca Virtual en Salud (http://regional.bvsalud.org/) was created in March 1998 as an initiative of the Pan-American Health Organization (a WHO affiliate). Its mission was to improve access to reliable, locally relevant information on health and health sciences. Pathology journals from Ibero-American countries were included as part of this library.

2000-Present

Telepathology, WSI, and Image Analysis

The year 2000 was a highly significant year for telepathology in South America. Early that year, the UNC, the Instituto Tecnológico de Electrónica y Comunicaciones and TELECOM (National Company of Telecommunications in Colombia) began a pilot study on telemedicine. This study connected the San Andres Islands, Amazonas, Bogotá and other centers. Telepathology services were based on the use of the Nikon Coolpix 995 digital camera and Nikon and Leica microscopes.[141] The inaugural Telemedicine Meeting in Panama took place in August 2000, with the collaboration of Dr. Ronald Weinstein. In this meeting, the National Program of Telemedicine, with the participation of the Medical School of the Universidad de Panamá presented a telepathology project led by Dr. Silvio Vega that connected the Universidad de Panamá with the Hospital El Vigia in Chitré.[159,160] Finally, in October 2000, an international randomized telepathology study was performed between Instituto Materno Infantil de Pernambuco in Brazil and St. Jude Children's Research Hospital in Memphis, Tennessee, USA. The main objective of this project was to improve the diagnostic accuracy of pediatric cancer using static telemicroscopy. It was concluded that telepathology is an efficient second opinion method and that it also allows for an improvement of quality and speed of diagnosis, resulting in a better treatment of cancer in children.[161]

In 2001, tele-consultations utilizing static telepathology only were performed between the Arias-Stella Pathology and Molecular Biology Institute in Peru and the Instituto Nazionale per lo Studio e la Cura dei Tumore in Milano, Italy. These tele-consultations were a success, with concordance rates similar to previous studies on static telepathology.[162] The Arias-Stella group continues to be a driving force for telepathology in South America to the present day.

Between 1st October 2003 and 30th September 2006, the European Union funded the T@lemed project. This project – which promoted evidence based telemedicine for remote and rural underserved regions in Latin America using e-health platforms – included fast transmission of microscopy images from local hospitals to high-level referral hospitals, in order to improve the diagnosis of malaria. There were 14 institutions from many different countries that participated in this project, notably the Universidad Santiago de Cali, Universidad Nacional, Centro Internacional de Vacunas and Cámara de Indústria y Comercio Colombo-Alemana of Colombia and the Fraunhofer Society of Germany.[163]

In 2004, Dr. Mauricio Ribeiro Borges of the Pontifícia Universidade Católica do Rio de Janeiro published a comprehensive thesis on telepathology.[164] This thesis would later be recognized as a classic in the field, and now serves as one of the cornerstone texts in the understanding of telepathology in Latin America.

In 2005, the ABC Hospital of Mexico was formally recognized as a private institution with one of the highest technological levels in telepathology and digital medical imaging services in the Latin American sphere. It has remained a regional superhub for pathology informatics endeavors ever since.[145] Also in 2005, two microscopes with attached digital cameras were installed at the National Cytology Program of El Salvador, allowing quick consultations between pathologists in remote areas of the country and experts in San Salvador.[4]

In 2005 in Colombia, a telemedicine network between Cali (Universidad Santiago de Cali) and Costa Pacífica was developed for the tracking of infectious diseases. Microscopic images containing blood and urine samples were exchanged utilizing a custom store-and-forward architecture. This network is still in operation today.[165]

In 2006, the Amazon Telemedicine Project developed a tele-health system using satellite-based networking to reach Amazon Indians in Northern Brazil, with applications in the areas of telecardiology, teleradiology, teledentistry, telepathology, and videoconferences. The telepathology component of this project largely focused on the transmission of high-resolution static images of Pap smears. The satellite communication system – said by its creators to be highly robust, and cost-effective – is still in operation and actively use today.[166]

In 2007, a Peruvian project known as PAMAFRO (Control of Malaria in Border Areas of the Andine Region) began installation of wide-area networks utilizing IEEE 802.11 (Wi-Fi) technology in remote areas of the country. One of the networks – which spans a 447 Km segment along the Napo river, allowing an uplink to the Hospital Regional de Iquitos – is notable as being the single longest known Wi-Fi network in the world.[167]

In 2007, the BioIngenium Research Group of the UNC in Bogotá, Colombia was formed. It has since then made virtual microscopy, image compression, and image analysis its main research foci.[168] One of its notable projects has been on the automatic programmatic detection of malaria parasites in thick blood films stained with haematoxylin-eosin.[169]

In 2008 in Cuba, a national network for telediagnosis in anatomic pathology was established by a National Reference Center for Anatomic Pathology (CENRAP) in the Hospital "Hermanos Ameijeiras" in La Habana, Cuba.[170] That same year, in Cuenca, Ecuador, a private hospital known as the SOLCA Institute began to utilize a WSI scanner for tele-consultation and primary remote diagnosis. To the best of our knowledge, this is the first – or at least one of the first – mentions in the South American literature of WSI for primary diagnosis.[171]

Finally, in 2009, a telepathology pilot using digital slides created with Aperio ScanScope was performed with the participation of the Arias-Stella Pathology and Molecular Biology Institute in Peru, the Department of Pathology of University of Sao Paulo in Brazil, the Hospital Británico de Buenos Aires in Argentina, and Centro Consulenze Anatomia Patologica in Milano, Italy.[172]

Teaching and CME

In 2000, a website containing a comprehensive collection of histopathologic images with a special focus on oral pathology was published by the Fundação Odontológica de Ribeirão Preto, Universidade de São Paulo.[173] Also in 2000, the University of Cauca served as a mirror site for the 6th Internet World Congress for Biomedical Sciences, organized by the Pathology Department of Hospital de Ciudad Real in Spain.[174] Since June 2002, autopsies have been broadcast online on a weekly basis, with the participation of 12 Brazilian medical schools.[175]

In 2004 in Uruguay, the Pathology Department of the Medical School of the Hospital de Clínicas "Dr. Manuel Quintela" in Montevideo, Uruguay started publishing online study material for medical students.[176] In 2005, the Virtual Hispano-American Congress of Pathology began utilizing WSIs instead of static images in its presentations. Finally, at present, iPath hosts the Telemedicina Sur telemedicine network, active in South-American countries for medical discussions, including pathology CME and consultations.

LISs

In the last 5 years, significant improvements have been made in data management in pathology departments in Central and South America. Several commercial vendors (e.g., Labsoft Tecnologia Ltda.) are distributing products in Argentina, Brazil, and other countries. System integration and interoperability solutions for pathology are also available in products like data innovations (Austria and Brazil), Tesi Pathox (Italy and Brazil), CSC Patwin, Vitro Novopath and Esblada Gesapath (Spain and Ibero-America). Tracking and laboratory connectivity solutions from Dako (DaloLink, TPID) are also distributed in Brazil and other Ibero-American countries.

ASIA

The progress of pathology informatics in Asia has been much like the phenomenon of watching ripples spread across the surface of a once-placid pond after a pebble has been thrown into it. The pond in this metaphor is Asia; the pebble represents progress in telepathology and WSI from the West. Although this historical review of informatics in Asia is focused largely on advances in digital imaging, much progress has been achieved in these countries utilizing computers to establish LISs. In general, development of digitized telepathology was supported by the development of computers, and improvements in the performance of digital cameras. In the modern era, WSI have been a primary focus of pathology informatics activity across the world. Asia is no different in this respect. In some Asian countries (e.g., Japan), where network infrastructure and high-speed Internet-based telemedicine are well-developed WSI systems are in heavy use. In other Asian countries (e.g., China), there are significant bottlenecks to further penetration of telepathology, including (i) low levels of understanding in society in general about the importance of pathological diagnosis, (ii) physical constraints, including infrastructure development not keeping up in large geographic areas, (iii) high prices of WSI systems, (iv) lack of mutual trust between pathologists in different areas, and (v) regulatory issues.

The story of digital imaging in pathology was, in its earliest years, confined largely to the USA and Europe.

With the development of the Internet came the possibility of sending and receiving digital images across the world; most historians of our still-nascent field trace the lion's share of the evolution of the current state of telepathology – and indeed pathology at large – to this singularly disruptive event. Many organizations – such as the AITN – sprang up in the so-called "Web 1.0" era, providing platforms for diagnoses and consultations based on international telepathology involving not only the USA, but also many other nations, including China and Japan.[177] While these early efforts uniformly used static telepathology as their primary diagnostic modality, in the modern era we have seen a shift to the usage of WSI instead.[178] In Asia, the story of true digital pathology has just begun; it currently lags far behind the more developed state of digital pathology among the Western nations. However, Asian nations – particularly those with advanced network infrastructures like Japan and South Korea – are making more and more use of digital pathology as broadband saturation in these countries have reached (and indeed by now have exceeded) 100%. More recently, fast-growing economies like China and India have been pushing forward with digitization. Iran and Uzbekistan are also promoting digital pathology.[179,180]

Telepathology options differ from country to country: Offerings run the gamut from relatively slow transfer of static images taken by digital cameras via digital subscriber line to nearly-instantaneous transfer of WSIs via fiber optic networks.[181-183] Governmental support for telepathology and digital pathology is also quite variable – some countries have embraced these new technologies as quickly as they are introduced, whereas others have applied heavy regulation that has effectively stifled the growth of digital pathology in those nations. A case in point is the comparison between Japan and South Korea: Although both countries have impressive network infrastructures (South Korea's broadband penetration approached 100% as of 2012), the uptake of digital pathology in South Korea has been relatively slow due to an onerous regulatory environment. Compare this to the governmental policies of Japan, which openly promote a "standardization of cancer medical services" based on WSIs as well as other medical advances. It should therefore, come as no surprise that Japan's growth in telepathology and WSI adoption is outstanding as compared to that of South Korea – a nation that not only has a smaller landmass, but also an arguably better-developed network infrastructure [Figure 9].[184]

Japan

Japan's network infrastructure is among the best-developed in the world. Population coverage and network speeds also rank among the highest in the world-it is worth noting that fiber optics is a common connectivity option even among general households! High-speed network-based telemedicine has been developed to such a level that intraoperative rapid diagnosis and consultation take place actively in the field of pathological diagnosis. The first reports of digital pathology in Japan date from the first half of the 1990's. At first, static images were the major telepathology modality; now, real-time remote control of robotic microscopes and access to WSI is the norm. The essential driver of this change is widely accepted to have been the government's policymaking.

Infrastructure

Telepathology in Japan was first conducted on an analog system. It started shifting to digital modalities in approximately 1996 by using the ISDN protocol, which was the first step toward full implementation. In 2001 and 2002, asymmetric digital subscriber line (ADSL) and fiber optics, respectively, were implemented in telepathology. The advances in transmission technology combined with wide spread digitization made it possible to transfer still images and videos of tissues for pathological diagnosis. With the more recent addition of Hi-Vision (HDTV) technology, intraoperative rapid diagnosis is performed utilizing dynamic methods with full remote control of a robotic microscope.[185,10] WSI is also utilized for consultation and second opinions while their application in medical education is expanding. In 2009 and 2010, the high-speed satellite "Kizuna" was used for the first-ever Japanese fully dynamic/WSI telepathology study via satellite; this study allowed for simultaneous live telepresence across three sites (Iwate, Tokyo, and Okinawa).[186]

Digitization

In Japan, the static, dynamic (live video feed without control of the microscope), fully dynamic (live video feed with direct control of robotic microscope), and WSI methods of digital pathology are all in use. As of today, two Japanese providers offer fully dynamic and/or WSI methods. The Ministry of Health, Labour and Welfare has provided (and continues to provide) half of the funds necessary to procure WSI scanners and other such equipment at institutes and hospitals across the nation. The total number of WSI systems deployed in Japan is approximately 400, most of which are provided by Hamamatsu Photonics and Olympus. The use of WSI has taken root not only for pathological diagnosis, but also for education. The usage rate in medical faculties of Japanese universities for teaching histology and pathology is 46%.[187] Most of the universities utilize WSI in combination with existing microscopes; however, depending on the content of the lectures, some have fully shifted to WSI.[188] Although a complete shift from microscopes to WSI still requires validation of their educational effectiveness, WSI has been highly praised by students and researchers alike as they allow more than one user to look at a specimen simultaneously and to conduct discussions among themselves. WSI is also more flexible compared with traditional microscopes.

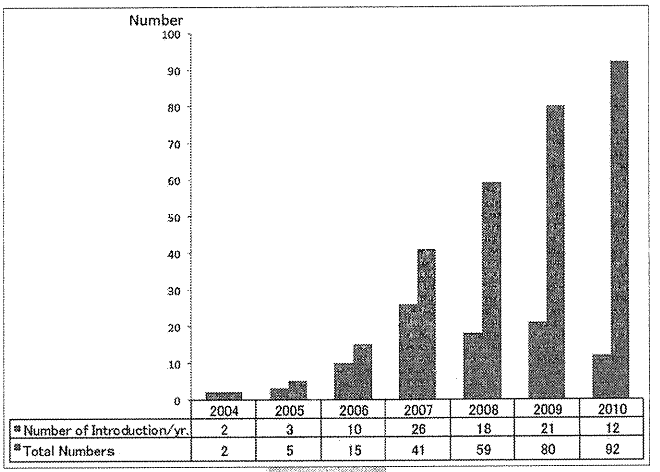

Figure 9: Growth in Japanese telepathology installations, 2004-2010

China

Expectations for telemedicine including telepathology are very high in China, which is a country with an extensive national territory. Telepathology, however, is not currently actively practiced because (i) the infrastructure has not developed fast enough to cover all areas, (ii) hardware cost is still high, (iii) digital imagery is not fully trusted, (iv) people have a strong attachment to traditional optical microscopic diagnoses, (v) not enough physicians engage in telepathology, and (vi) state regulations concerning remote diagnosis are inadequate. In terms of infrastructure, digital subscriber line (DSL) is still the dominant technology, but more recently some cases of telepathology are reported as using fiber optics and WSI.

Infrastructure and Equipment

Along with its recent outstanding economic growth, China has been rapidly expanding its infrastructure. The speed of development can be exemplified by the number of Internet users reaching 400 million in 2011 and the number of cell phone users reaching 900 million.[189,190] Nevertheless, China's overall network infrastructure remains less developed than that of the USA, Japan, and South Korea. Although the absolute number of people who have access to the Internet is the highest in the world, if divided by China's large population, the penetration rate remains as low as 36.3% as opposed to 100% in South Korea, 78.3% in North America, and 78.4% in Japan.[191] Moreover, the digital divide in terms of Internet use between urban and rural areas is significant.

Digitization and Telepathology

Pathologists are scarce in China, particularly in the southwest region. To ascertain the telepathology situation in the country, we performed a PubMed search with the keywords, "'Telepathology" and "China."' There were five hits, three of which were related to consultation using the AITN as reported by Weinstein. These telepathology cases utilized static telemicroscopy over the Internet. Telepathology efforts indigenous to China, however, began in the first half of the 1990's.[177] Since the early 2000's, telepathology studies have been conducted based mainly on employing digitized still images and live video feeds without direct microscope control. These two diagnostic modalities appear to be the current mainstream in China. More recently, however, telepathology using fiber optics and WSI has tentatively begun between

Peking University and its first hospital. The most popular way of currently conducting telepathology in China is to either share WSI on a server with a trusted partner or to send an E-mail with a WSI as an attached file in the file transaction hub (FTH) format via DSL. In this format, the sender observes an image enlarged by a factor of four, extracts his/her area of interest into a 40-times-larger WSI, attaches the image as an FTH file to an E-mail, and sends it to the consulting pathologist. The advantage of this process is that the WSI files are of relatively small size, between 2 MB and 30 MB. This represents a middle ground between WSI-based and static image-based approaches. The attempt started with validating the result of this mode of telepathology by comparing it to conventional optical microscopy using biopsy cases; the diagnoses were reported to show good agreement for all cases.[188,189] Nevertheless, the use of static telepathology still remains more prevalent than dynamic methods. In addition, the issue of disparity between urban and rural areas remains unsolved in terms of limited infrastructure development and utilization of Information Technology (IT) in hospital facilities. As such, the practice of telepathology in China is currently limited to certain institutes only.

India

Telepathology in India is generally limited to static telemicroscopy utilizing the Internet.[191] Similar to China, constraints include the size of the country, the gap between urban and rural areas, startup cost, a power grid electrical supply system that is subject to occasional blackouts, and also the complex human relations among several groups.

Infrastructure

Due to India's historical background, the Indian people exhibit a high level of proficiency in English and mathematics, and the implementation of IT, mainly in enterprises, has been well positioned in a global society since the 1990's due to the government's policies. As of June 2010, the number of subscribers to wired Internet services was 16.72 million and that to broadband services was 9.47 million. The most popular connectivity type is DSL.[192] At the same time, the number of cell phone users reached around 635 million. The (what?) coverage was approximately 53.8% in 2010.[193] The country is pushing forward the construction of a wireless communications infrastructure in rural areas, with increasing adoption of third-generation (3G) wireless telecommunication and WiMAX technology.

The implementation of IT in medical settings is observed in the connection of the three major municipal hospitals in New Delhi with their affiliated hospitals, and communication with local cities was experimentally attempted in the Hyderbad District in the Southern part of the country.[194] Transmission of surgery-related images and other interactions on remote images in other districts have not been reported.

Digitization

According to the 50th Annual Conference of the Indian Association of Pathologists and Microbiologists held in Mumbai in 2001, the static (store-and-forward) method of telepathology relying on the Internet was used for consultation.[191] This static approach is still the mainstream method of practicing telepathology, but is used only by very few pathologists. Desai *et al.* successfully obtained effective tele-consultation outcomes by connecting the Tertiary Cancer Center (Tata Memorial Hospital) and the Rural Cancer Hospital (Nargis Dutt Memorial Cancer Hospital). However, these consultations were performed with a 56 kbps modem, which is not broadband. Still, concordance rates from this trial were 90.2%, and such time- and labor-consuming efforts are contributing to the rise in the level of confidence in telepathology.[195] In 2011, Kanthraj reported the application of store-and-forward teledermatology and mobile teledermatology.[196] The scope of this application, however, mainly covered macroscopic observation and treatment and addressed pathology images only in part. The promotion and utilization of WSI in the country awaits better infrastructure and other issues are overcome.

South Korea

The adoption of IT in South Korea is characterized by the highest levels of high-speed Internet coverage in the world, cloud computing, and active applications in the medical sphere. Conversely, due to a heavy regulatory environment and the high number of diagnostic pathologists to the number of hospitals, social need for and interest in telepathology seem marginal. The number of WSI scanners is approximately 30, which is fewer than Japan has, and most are being used for educational purposes.

Infrastructure

The country has been developing its infrastructure for high-speed Internet based on advanced DSL technology, as part of its initiative promoting IT projects since the mid-1990's. A great portion of the South Korean population is concentrated in Seoul and its metropolitan area, where many people reside in housing complexes. This is an appropriate environment for ADSL, and its coverage has expanded due to its low pricing, which since its introduction has fallen even further as a result of fierce competition among providers. Today, more than one-half of wired broadband subscribers use fiber to the home and optical LAN with sustained transfer speeds of greater than 50 Mbps.[197]

In general medicine, receipts (medical fee bills) and other documents have been increasingly digitized, such that the nationwide digitization rate for medical billing was already 88% in 2006 and almost 100% of this

information has been made available online at dispensing pharmacies.[198] Nevertheless, telemedicine is observed only in the government's primary-level research and not in practical settings due to legal constraints.

South Korea is a rapidly aging society, just like Japan. Thus, the "u-healthcare" industry, which combines information and communication technology with medicine, garners much attention for future healthcare services. This concept includes telemedicine and also remote health control. It is most likely that, once the regulations are relaxed, services at an international standard will immediately be available in South Korea, where the IT infrastructure is well established.

Digitization

Though the number of WSI systems in South Korea is smaller than that in other Asian nations, WSI is being applied in educational conferences, but rarely for telepathology. Factors contributing to this include the South Korean medical laws and also the perceived lack of need for telemedicine considering the relatively large scale of South Korean hospitals and the presence of local pathologists. WSI for educational applications, on the other hand, are widely observed and enthusiastically adopted in the hands-on training of students and for self-study. WSI is highly appreciated by students and positioned as an important tool for pathological education.[199] It is likely that the WSI-based learning style will be common in the country, where onsite LAN is well developed in educational settings.

AUSTRALIA

Australia's Council for Scientific and Industrial Research Automated Computer Mark 1 (CSIR MK1), which ran its first program in 1949, was the fourth stored program computer in the world. This and the replacement machines in Sydney, SILLIAC and KDF9 were used for medical and pathology research including Fourier analysis of pressure and displacement waves to understand the elasticity of arteries. Between 1969 and 1971 three Australian preventive healthcare organizations began using computers for EHRs. All these systems included a pathology LIS. Those organizations were Medicheck and Preventicare in Sydney and the Shepherd Foundation in Melbourne. Medicheck, modeled on the Kaiser Permanente Multiphasic Health Screening Centre led by Morris Collen (after whom the American College of Medical Informatics Prize is named), had its own pathology laboratory and installed the IBM 1800 while Preventicare, which developed into New South Wales' largest private pathology laboratory, used the IBM Call 360 time-share service. Both developed their own software. This was front-page news at the time and seen as a threat to good medicine. Around the same time an LIS written in assembler on ICL hardware (Hospro) was developed and became the dominant system in private pathology practices in Australia. These LISs were later replaced by one of the world's first LISs that used a high transaction relational database-Triple G's Ultra (so-called after the three Australian developers who called one another George but were actually Mike, Peter and Brian). Triple G sold in Canada and the USA, and the company was subsequently acquired by GE.

Other LISs developed in Australia of note are:

- MGH Utility Multi Programming System (MUMPS) based system first developed by Détente in 1970's and now known as ISS-Omni-Lab installed in the United Kingdom and New Zealand. This was redeveloped by Sonic into their Apollo system which is now in use in their laboratories around the world.
- Pick based system from last resort support which is sold into the United Kingdom.
- Delphi and HL7 based kestral and medical objects LISs-both organizations at the vanguard of informatics standards development and recognized for having contributed significantly, especially to HL7.

The first electronic transfer of pathology reports from laboratories in Australia was in 1969 using teletypes on the Preventicare IBM Call 360 network. In the early 1970's, this network got as large as 250 sites in four states and was reputed to be the third biggest network of its kind in the world.

The first pathology transfer using the Internet was in the early 1990's, but the most common method then was modem to modem communication. In 1993, a *de facto* standard for this purpose was introduced with an agreement between two dominant Queensland laboratories. This was a FORTRAN like message called Pathology Information Transfer (PIT) that was and still remains in wide use. In 1996, a Standards Australia Committee (IT 14-6-5) was established ostensibly to answer which was the best Standard for Australia to adopt for pathology results reporting-PIT, EDIFACT or HL7?

In 1997, Standards Australia established a relationship with HL7.org (and later HL7 Australia) and in 1998 Australian Implementation Standards AS4700.1 ADT and AS4700.2 for Pathology Orders and Results were published. A detailed handbook for pathology messaging (HB262) followed in 2002. The Standard pointed to a subset of LOINC codes as the recommended terminology for the test name (OBX3). This standard for electronic communication was taken up in the National Pathology Accreditation Advisory Council "Requirements for Information Communication" publication in 2007, and so forms an integral part of the requirements for laboratory

accreditation in Australia. It is estimated that there are around 100 million pathology messages a year and it is now the usual manner for delivering a report, and in some places now also used for ordering.

In 1993, the Australasian Association of Clinical Biochemists sponsored a satellite meeting of the International Federation of Clinical Chemistry and Laboratory Medicine dedicated to pathology informatics at Uluru in the middle of Australia. Among the eminent invited speakers were Dr. Octo Barnett from the MGH, who was instrumental in designing and programming one of the first comprehensive HIS. This was followed by a meeting a decade later sponsored by the Health Informatics Society of Australia and in 2007 the first World Congress in Pathology Informatics co-sponsored by the API, the Health Informatics Society of Australia and the Royal College of Pathologists of Australasia (RCPA).

Pathology informatics research and projects reported at these meetings and subsequent ones included:

- The application of ripple-down rules in pathology decision support (1993)
- Privacy in community pathology (2002)

Government Quality Use of Pathology Committee Projects (2003-2007):

- The chain of information custody
- The role of pathology informatics in a quality framework
- The influence of computers on ordering
- Terminology
- Electronic reporting and ordering
- Natural language processing of surgical pathology reports
- Evaluation of pathology order entry systems in hospitals
- A seminal work on Infectious disease informatics (2009).

Unlike teleradiology, where Australia is a major player, telepathology has not yet become routine. Virtual microscopy, using Aperio, has however been a component of the RCPA Quality Assurance Programs since 2008. In 2007 a national workshop on safety and quality in pathology identified workforce and smart requesting and reporting as three of the top five issues that should be addressed in Australia. This set the agenda for funding through the Quality Use of Pathology Program of the Australian Department of Health and Ageing. The role of the health informaticist was recognized in the 2008 report entitled 'The Australian Pathology Workforce Crisis' and has been included in workforce considerations since. In 2012, the RCPA established a formal Informatics Advisory Committee of the same status as other sub-disciplines in pathology after having had ad-hoc taskforces for many years.

EUROPE

Stereography and the Infancy of Pathology Informatics

In the infancy of pathology informatics in Europe (1945-1970), much effort was focused on measuring sizes and numbers of nuclei, cells, vessels, glands and nerves by projecting microscopic images on a light screen equipped with a suitable grid.[200] This technique – later to be called stereology – would allow three-dimensional approximations to be extrapolated from two-dimensional measurements.[201] The history of stereology in pathology can be traced back to the 1950's, when H. Elias analyzed the structure of the mammalian liver,[200] and Tomkeieff and Campbell investigated in the structure of the mammalian lung.[201,202] Later, Cruz-Orieve applied rigorous mathematical algorithms to stereology, and Gundersen and Jensen published their ideas of the "fractionator", "nucleator" and "rotator" – statistical sampling techniques that allowed the observer to estimate particle volume and distribution in an unbiased manner.[203-205]

At that time, European research in pathology informatics was largely focused on attempting to associate stereological data with clinical findings, for example, morphological changes with cancer cell types, or to predict the survival of cancer patients.[206,207] Although several significant associations were reported initially, clinicostereologic correlation never made it past the experimental phase. On the other side, such experiments promoted further investigation and understanding of semi-quantitative methods in image evaluation, as well as research in classification, coding, and nomenclature.

Coding Standards and Natural Language Processing

Once the first computers became available, two important areas of research and development emerged: The standardization and codification of clinical nomenclatures (e.g., SNOMED, ICD) and natural language processing (and auto-coding) of free-text pathology reports.[208-213] These efforts quickly bore fruit and were integrated into routine pathology services. At the Institute of Pathology at the University of Heidelberg, for instance, there were projects to (a) enable "just-in-time" free text translation of autopsy findings and (b) pursue complete digitalization of all autopsy records back to 1841.[214]

The advent of computerized tomography technology in the 1980's induced a sharp decrease of autopsies. For instance, at the Institute of Pathology at the University of Heidelberg, the number of autopsies dropped down from 1200/year in 1970 to approximately 350/year in 2000; other European and German Institutes of Pathology displayed a similar trend.[215] It was around this time that

interest in natural language processing for the automation of pathology reports waned, instead being supplanted by research in molecular biology and genetics.[216-218]

The drop in autopsies did not diminish the workload of pathologists. In fact, the concurrent rise in biopsies, fine needle aspirations, and surgical specimens created an overwhelmingly heavy workload for pathology departments throughout Europe, along with the need for sophisticated logistics, financial analysis, and clinician-facing electronic communication tools in the laboratory.

Laboratory and HIS

In Europe, the increase in biopsies induced research in different aspects of pathology informatics. Questions on to handle the enormous number of biopsies and other specimens, how to classify the obtained diagnoses, and how to correctly manage issues of reimbursement arose,[219] eventually resulting in the need for the first precursors of modern LISs.[220] Advanced tissue testing modalities, most notably immunohistochemistry and DNA sequencing, drastically increased the complexity of routine tissue handling, in turn requiring a standardization of laboratory techniques and performance.[221] It was soon recognized that LISs themselves require regulation and standardization, which gave rise to formal certification of LISs. Such certification is now considered to be mandatory since the beginning of this century.[222,223]

At the same time, similar factors in the health care industry at large forced hospitals to introduce electronic record-keeping systems, and thus HIS were increasingly adopted in the 1990s.[224] In Germany, LIS and HIS are strongly controlled by obligatory insurance companies: employees who earn less than a certain salary per month are mandatorily insured by one of these companies. These companies provide reimbursement for care which is calculated by so-called reimbursement codes (codes for diseases, therapeutic and diagnostic examinations, all of which correspond to a flexible, fixed amount of Euros). The financial value of each code is locally and periodically regulated and depends mainly upon the local and momentary contribution of the insured workers to the insurance company. Thus, the management and maintenance of LIS and HIS in combination with the demands of certification is highly region-specific. Commonly, these systems require an update every 3 months.

With only a few exceptions, all patients in Europe have been equipped with an insurance card. These cards commonly integrate a solid-state electronic storage component that contains the patient's personal identifiers and the patient's insurance company. While these cards have carried no medical records up until now, trials are now underway to include comprehensive medical records on insurance cards.[225] In most cases, these data can be electronically transferred into the HIS, and afterwards into the LIS in hospitals, or into the local administration system of private pathology institutions. This allows for true portability of a patient's personal health records, as well as easy billing and reimbursement on the part of the institution.[225]

LIS and HIS are well developed in nearly all Western European countries including Belgium, Denmark, Finland, France, Great Britain, Iceland, Ireland, Italy, Norway, Portugal, Spain, Sweden, and the Netherlands. Those in former socialistic EU countries such as Estonia, Latvia, Lithuania, and Poland have introduced well developed LIS and HIS in combination with the mandatory renovation of their bigger hospitals.

The implementation and maturation of LIS and HIS was forced by the demands of public health and the government. Standardization of image transfer (in radiology) and medical records inside and in between different hospitals were considered to be prerequisites for success. The implementation of PACS and that of DICOM standards occurred in the middle to end of the 1990's. At present, more than 80% of hospitals and private institutions (radiology practices) are assumed to be equipped with such systems to the best of our knowledge.

Image Analysis

The development of measurements at a light microscopic magnification was characterized by three milestones in the 1980's-1990's, namely the development, implementation and standardization of DNA cytometry, syntactic structure analysis, and communication in diagnostic pathology.

DNA cytometry was the first and to our knowledge only pathology measure that introduced fixed, reliable, and commonly agreed measurement standards and error limitations, for example, a standard deviation of less than 5%, and others.[226-229] It is a crude measurement procedure of genetic abnormalities in a nucleus (total amount of DNA) and is based upon the stoichiometric light absorption of Feulgen stained DNA. The analyzed parameters include ploidy, S-phase, and 5C exceeding rate.[226-229] In recent years, DNA cytometry has been replaced by genetic examinations that permit a more detailed insight into chromosome, genes, DNA sequences, and proteins.

Syntactic structure analysis is a measure of structures present in cells (or nuclei). It utilizes graph theory to successfully analyse and annotate properties between nodes (edges) in combination with properties of nodes (vertices). It can be considered as a direct successor to DNA cytometry.[230-234] The reported results and derived data (e.g., Structural Entropy) have been shown to be of prognostic significance for certain patient populations, most notably lung cancer patients with intra-pulmonary metastases.[235-237] At present, the technique has been expanded to IHC images, and reported being suitable for determination of so-called areas of interest in WSI.[238-241]

Telepathology

Early Events Prior to the Internet

The history of telemedicine is closely associated with the technological development and progress in medical diagnosis and treatment.[242,36] Most efforts focused on diagnosis (teleradiology, telepathology, teledermatology, tele-endoscopy, etc.), and only a few investigations were devoted to teletreatment such as telesurgery.[242,36,243-246,178,247] The floodgates of telemedicine were opened by the National Aeronautics and Space Administration of the USA in the 1960's.[245,178,248-251,177,252-255] Telemonitoring systems had to be implemented in order to monitor the health condition of astronauts.[256-263] These included continuous monitoring of cardiovascular functions as well as those of brain functionality.[242,253,264,265] Based upon these experiences, earth-bound telemedicine trials were performed in the USA first. One of the earliest events was the video transmission of black and white blood smears from the Logan International Airport, Boston to the MGH by W. Beck and K. Bird in 1968.[245,254,266,267] Despite some tele-education and distant cytology consultations done at John Hopkins Hospital, Baltimore, USA (J. Frost)[268-271] in 1979, it took about another 20 years until further investigations in telemedicine followed. They started with USA-based trials.[266,140,272,273] European investigations followed about 3-4 years later.[273,274-279] At that time, telemedicine was based mainly upon still images, and those that were performed using the *remote control systems (mainly for intra-operative frozen* section). These considerations are based upon the three different types of tissue-based diagnostic needs (pre-, intra- and post-operative diagnostics.[36,280-286] With the exception of cardiology, most investigations regarding telemedicine trials included still images.[247,248,252,287-299] Still images for telemedicine investigations were seen also in radiology (including ultrasound examinations), surgical pathology, and dermatology.[247,276-278,295,298,300-311]

Telecardiology, however, did not include still images, as it relied on the transmission of analogue signals. In fact, the first telecardiology trial was reported by Wilhelm Einthofen (1860-1924), who in 1905 transmitted heart beats by telephone.[312-315]

This historical event remained silent for more than 50 years until the need for bridging long distances of inaccessible heart functions was evident for astronauts. In *Europe, the electronic transmission of electrocardiogram* signals to specialized clinics took place in the 1980's. The analogue signals were acquired by specific electronic devices (frame grabbers) and the patient could be monitored for at least 24 h.[295,313-316] Ultrasound telemedicine devices had already been suggested in 1978.[313-320] However, it was only in the 1990's that these emergency devices were available for patient care in Europe.[250,264,265,310]

The common telecardiologic devices included ambulatory Holter monitors and loop event recorders, or event-triggered monitors. Similar to other telemedicine fields the preferred solutions have been an end to end connections, i.e., a fixed client – observer line.[250,265] In addition to telecardiology, the development of telemedicine applications in Europe was formed by other medical fields that use images for diagnosis, such as dermatology, pathology, and radiology.[177,316,321-325,327-341]

Intensive research to explore the potency of this new *technology was remarkably enhanced by the on-going* technological development. Here, three different "coordinates" have to be mentioned:

- Velocity and the kind of line (telephone) connections available,
- Systems of image acquisition and display, and
- Electronic communication systems.

To start with, telecommunication in Europe was characterized by a unique situation in which state owned telecommunication companies dominated the market. Private telephone companies did not exist at the beginning of the telemedicine era. Therefore, the analogue lines could be replaced by digital line connections without major difficulties or without dealing with (intra-state) different digital standards. The ISDN was created by the European Telecommunication Standards Institute in 1989 and implemented as a European Telecommunication Standard in 1993.[342]

European efforts with telepathology started, however, prior to this development. Of particular interest was the immediate transfer of a (primary) diagnosis in surgical pathology during frozen section. This involved the replacement of specimen transportation from smaller hospitals, which were not equipped with an Institute of Pathology, by the electronic transfer and remote control of microscopic images.[121,343-351] Several specific telepathology systems have been developed for this purpose.[345,350,352-357]

In 1988, a routine telemedicine service was started by T. Eide and I. Nordrum to provide three smaller hospitals with an intra-operative frozen section service.[334,350,355] The hospitals were located at a distance of 300-400 km from the Institute of Pathology of the University of Tromsö, Norway. A specific end-to-end user (store-and-forward) system was developed. By 1993, *more than 150 intra-operative frozen section diagnoses* had been reported through this service.[275,122,359] At the same time, the University Hospital of North-Norway performed trials in teleradiology, teledermatology, tele-otorhinolaryngology (remote endoscopy), remote

gastroscopy, tele-echocardiography, remote transmission of electrocardiograms, telepsychiatry, teleophthalmology, teledialysis, tele-emergency medicine, tele-oncology, telecare, telegeriatrics, teledentistry, and maritime telemedicine.[291]

Telepathology trials confirmed the following:
Intra-operatively obtained microscopic images could be acquired with an image quality that was sufficient for reliable diagnostic purposes.

The velocity (bandwidth) of the (analogue) telephone line connections permitted a stable transfer of images.

The diagnostic error rate of this technology was in the same range as that of conventional light microscopy frozen section technology, which served as the gold standard.

Patients greatly benefited from this technology by being treated in accordance with the latest guidelines, by avoiding the need to be transported over a long distance, and minimizing their risk of potential repeat surgical treatment.

The costs of this technology could be compensated by using reliable intra-operative diagnostic statements that translated into potential financial reimbursement.

The impact of the Tromsö trials on the development of European telemedicine (pathology) cannot be overstated.[242,360-363] Several telepathology teams followed suit with their own investigations on the use of this technology to support a remote frozen section service, and reported similar results.[298,332,343,346,351,357,364,365] This applied technology seemed to be promising, and was considered to increase the reputation of smaller hospitals, helped to establish larger institutes of pathology which would take over the services of smaller institutions, and provided patients with the latest technology for medical diagnosis and treatment. At about the same time, in 1990, Kayser *et al.* reported on different aspects of telepathology.[36,249,255,338,360,362] They performed the first expert consultation trials in Germany between Darmstadt, Heidelberg, and Mainz, three cities each with about 120,000 inhabitants [Figure 10], which was followed by the first quality control board examination of lung cancer cases using telemedicine in 1992.[56,362,363] The year 1992 can be considered to be one of the milestones of early telemedicine in Europe because:

- The Tromsö telepathology group reported their successful trials
- A unique telepathology network was installed in France by E. Martin, P. Dussere, and G. Brugal
- The first European conference on telepathology was held in Heidelberg
- The first international conference of telemedicine took place in Tromsö, Norway.

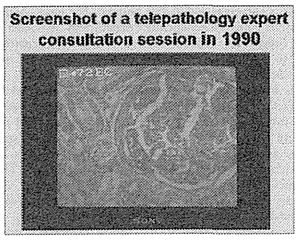

Figure 10: Demonstration of image quality of first expert telepathology trials in Germany, 1990. Note the breaks of line connections

These two aforementioned conferences solidified the acknowledgement of telemedicine in Europe, and all subsequent annual national conferences of pathology since 2002 included telepathology in their themes. Bi-annual European telepathology conferences were held without exception in:

- Heidelberg (Germany, 1992)
- Paris (France, 1994)
- Zagreb (Croatia, 1996)
- Udine (Italy, 1998)
- Aurich (Germany, 2000)
- Heraclion (Crete, Greece, 2002)
- Poznan (Poland, 2004)
- Budapest (Hungary, 2006)
- Toledo (Spain, 2008)
- Vilnius (Lithuania, 2010)
- Venice (Italy, 2012)

During the decade 1990-2000, there were several innovative European trials, some of which were successful, others not. Innovation by itself, however, does not assure success. The technological environment has to be mature in order to accept disruptive efforts, and to provide the "soil of success".[354] One successful application was the implementation of telepathology in a modern pathology laboratory in Cambodia, where a Cambodian-Thai-German pathologist team formed a working group (DIAG_AID) and trained Cambodian colleagues in diagnostic surgical pathology.[242,380,385] Only three experienced Cambodian pathologists were working in Cambodia at that time. A telepathology system was implemented at the Sihanouk Hospital Center of HOPE in 2002. It relied on the iPATH servers and was in use until the termination of the overarching iPATH system.[14,386,387] This infrastructure served for both assistance with immediate diagnoses and continuous education of young colleagues. The European assistance

was continuously accompanied by Thai colleagues. The first double blinded study on intra-operative frozen section telepathology was performed by H. Guski at the Institute *of Pathology, Charite.*[242,383,394,395] *This study confirmed* that digital images could be judged with the same diagnostic accuracy as conventional microscopic images. An additional innovative successful trial was the European founded Europath project headed by Dr. G. Brugal and Dr. K. Kunze.[388-393] To our knowledge, this was the first telemeasurement system in cytology (using static DNA analysis of Feulgen stained nuclei). It was started in 1996 and was fully implemented in 1999. It was employed for determining individual measurements, as well as analysis of measurement accuracy of both submitted microscopic images and commercial DNA measurement systems. A less successful trial was the introduction of the PARIS project (pathology and anatomy review international score) in 1999. The focus of this project was to peer review potential scientific articles and to provide the authors with an internationally acknowledged score independently from the journal in which the authors wanted to publish their *article. Only a few authors participated in this free service.* The project resulted in the first solely electronically published medical journal (the electronic Journal of Pathology and Histology), which was eventually cancelled due to lack of subscribership.[56,325]

The Internet Era

The advent of the Internet significantly influenced the development of telepathology in Europe.[344] Contemporary with the development and implementation of the Internet, preliminary development of the first WSI scanners started.[327,396-403] Both technologies impacted the application and distribution of telepathology; the Internet made telepathology easy to use which levelled the playing field between expert and non-expert computer telecommunication users.[242,327,368,404-409] Whereas in the pre-Internet era the implementation and maintenance of a telepathology network required high technical expertise and financial investment – thus sharply limiting the number of sites that could support telepathology – the Internet changed this allowing groups to implement telepathology platforms built from open-standards roots.

iPATH – developed by Brauchli and Oberholzer at the Institute of Pathology, University of Basel – is perhaps the most successful of these platforms.[367,14,13,410] It was first implemented in 2002, and has served over 150 user groups around the world. More than 15,000 telepathology cases have been examined using this system. Its success can be attributed to the basic operating principle or iPATH: the development of an easy to use system optimized for diagnostic consultation in pathology that also permits the creation of individual "working groups" (for example, specialized for cytology, lymphomas, or countries such as Cambodia, etc.).[386,387,13] Participating experts were notified about a client's request to remotely view a case via E-mail, and after rendering their opinion, the client was in turn notified via E-mail. The iPATH system was built using only open source software; due to this, local iPATH server installations were located all over the world.[59] Two similar Internet-based telepathology platforms were created during this time period, one in the USA at the AFIP (Washington, DC),[411-414] and the other at the Institute of Pathology, Charite, Berlin, Germany, sponsored by the Union Internationale contre le Cancre (UICC), Lyon, France called UICC-TPCC (UICC Telepathology Consultation Center).[396,407,415,416] All of these systems – including iPATH – have since been terminated. Two of them (iPATH, AFIP) have been replaced with commercial software packages. iPATH was the first telepathology platform to offer such tremendous flexibility, and as such enterprising individuals soon realized that it was possible to formulate something akin to a virtual department of pathology around it.[242,36,354] To accomplish this, administrators and pathologists were recruited; administration and duty plans were drawn up, and the first ever Virtual Pathology Institution (VPI) *was born.*[354] *This VPI served the total tissue – based* diagnostic needs of the Salomon Islands for several years.[417] Oberholzer and Brauchli implemented a pathology laboratory in the Solomon Islands and trained technicians to perform gross examinations on excised tissue create H and E glass slides and submit corresponding microscopic images to the VPI. Usually, a telediagnosis could be rendered within 24 h.[417] Prior to this solution, all tissue had to be sent to Australia, with an average turnaround time of roughly 2 months. This VPI was in operation for more than 5 years. It was, however, unfortunately terminated due to the fact that neither the Salomon Islands Government nor charity organizations were willing to consistently fund it. Nevertheless, this remarkable experience can be considered as proof that functional VPIs can be implemented.[354]

The recently (2011) released telepathology forum called Medical Electronic Consultation Expert System (MECES) is an example of a platform that has tapped into Web 2.0 and WSI technologies.[415] It focuses on performances experienced from iPATH and UICC-TPCC in combination automated electronic measurements (EAMUS™), still image acquisition, and WSI. In combination with an internationally well-known expert team, MECES will probably become a new milestone in the history of European telepathology.

CONCLUSION

The history of clinical (medical) informatics, a relatively new domain of computers and information science in healthcare, has been previously described.[419-421] However, to the best of our knowledge, this article represents the first account of the history of pathology informatics from a global perspective. Significant progress in our field has occurred in many countries around the world, and this rate of progress seems to be increasing. Progress in pathology informatics has been tied closely to developments in technology, particularly the advent of computers, the Internet and more recently digital imaging. It is apparent that major drivers in the field included the need for pathologists to comply with national standards for health information technology and for telepathology applications to meet the scarcity of pathology services and trained people in certain countries or underserved regions. Our predecessors are acknowledged for their insight, enduring investigations and trials to show us what works and what failed, and helping us solidify the current field of pathology informatics. This is a time of great excitement and opportunity for our discipline. Advances in genomic, molecular, diagnostic, imaging, and data analytic techniques have allowed – perhaps for the first time – a glimpse into a future in which hidden patterns embedded in our visual (e.g., WSI) and numerical (e.g., laboratory tests) data will be brought to light and exploited for the benefit of patient care. For us to face the challenges, and capitalize on the opportunities the "digital decade" of personalized medicine, it is imperative that we face our challenges and overcome ever changing barriers with the same vigor and excitement displayed by those who have gone before us. The history of pathology informatics is the story of us all. Those who have gone before us have left a rich foundation for us to build upon, but this story is not yet finished. We can be visionary leaders, bold explorers, and drivers of positive change throughout our healthcare systems; in doing so, we have the opportunity to take the destiny of medicine into our hands. Or we can be content to be followers or even ignore the disruptive changes that this history so clearly points out are looming before us; this being the path of diminishment and relegation to eventual irrelevance. We have the ability to write the end to this story. Where we go from here, is up to us.

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REFERENCES

1. Dafaallah K, Awadelkarim AA. Role of pathology in sub-saharan Africa: An example from Sudan. Pathol Lab Med Int 2010;2:49-57.
2. Graschew G, Roelofs TA, Rakowsky S, Schlag PM. Design and implementation of satellite-based networks and services for ubiquitous access to healthcare. In: Diodato N, editor. Satellite Communications. Rijeka, Croatia: Sciyo; 2010. p. 115-32.
3. Pachura P, editor. New knowledge in a new era of globalization. Rijeka, Croatia: Sciyo; 2011.
4. Hoenecke H, Lee V, Roy I. Pathologists overseas: Coordinating volunteer pathology services for 19 years. Arch Pathol Lab Med 2011;135:173-8.
5. Faravelli A, Garcia Rojo M, Guzzetti S, Yagi Y, Ferrari AM, Simonazzi S, *et al.* Pathologists overseas: a special session from the Patologi Oltre Frontiera (Pathologists Overseas) organization. Presented at the 11th European Congress on Telepathology and 5th International Congress on Virtual Microscopy. Venice, Italy: 6-9 June 2012.
6. International Telecommunication Union. Impact of telecommunications in health care and other social services. Geneva, Switzerland: International Telecommunication Union; 1998.
7. Hosch I. Investigation of the critical factors of success in telepathology: An international comparison study (dissertation). Konstanz, Germany: Universität Konstanz; 2011.
8. Adeyinka MB. Fundamentals of modern telemedicine in Africa. Methods Inf Med 1997;36:95-8.
9. World Health Organization. Report on the intercountry meet on telemedicine. Riyadh, Saudi Arabia: World Health Organization; 1999.
10. Achouri H, Achour N. Health services in Tunisia in the light of World Health Organization agreements. In: Casas J, Cassels A, editors. Trade in health services: Global, regional, and country perspectives. Washington DC: Pan American Health Organization Program on Public Policy and Health, Division of Health and Human Development; 2002.
11. Faravelli A, editor. Connecting Africa. Milan, Italy: Associazione Patologi Oltre Frontiera; 2008.
12. Schmid-Grendelmeier P, Masenga EJ, Haeffner A, Burg G. Teledermatology as a new tool in sub-saharan Africa: An experience from Tanzania. J Am Acad Dermatol 2000;42:833-5.
13. Brauchli K, Oberli H, Hurwitz N, Kunze KD, Haroske G, Jundt G, *et al.* Diagnostic telepathology: Long-term experience of a single institution. Virchows Arch 2004;444:403-9.
14. Brauchli K, O'mahony D, Banach L, Oberholzer M. iPath-a Telemedicine Platform to Support Health Providers in Low Resource Settings. Stud Health Technol Inform 2005;114:11-7.
15. Geissbuhler A, Bagayoko CO, Ly O. The RAFT network: 5 years of distance continuing medical education and tele-consultations over the Internet in French-speaking Africa. Int J Med Inform 2007;76:351-6.
16. Diallo O, Bayala R, Belem A, Sanou Li B, editors. Telehealth/telemedicine in Burkina Faso. Vienna, Austria: UNOOSA Scientific and Technical Subcommittee 47; 2010.
17. Wootton R, Patin NG, Scott RS, Ho K. Telehealth in the developing world. Ottawa, Canada: International Development Research Centre; 2009.
18. Ayad E, Sicurello F. Telepathology in emerging countries pilot project between Italy and Egypt. Diagn Pathol 2008;3:S2.
19. Worldwide Lab Improvement. Reporting on what god is doing 2004;8:1. Available from: http://www.wwlab.org/Spring_2004.pdf. [Last accessed on 2012 Aug 1].
20. Clemente C. Telepathology: support for the HOT (Hyperbaric Oxygen Therapy) project in the Allada hospital of Benin. Geneva, Switzerland: Abstracts of the Annual Meeting on Buruli Ulcer; 14-17 March 2005.
21. Baily A. It's plain sailing for instant diagnosis. Laboratory News 1 June 2005. Available from: http://www.labnews.co.uk/features/its-plain-sailing-for-instant-diagnosis/. [Last accessed 2012 Aug 1].
22. Mercy Ships. Fleet history. 2011. Available from: http://www.mercyships.org/au/our-ships.php. [Last accessed on 2012 Aug 1].
23. Bennani Othmani M, Diouny S, Balar K. Medical informatics in Morocco: Casablanca Medical Informatics Laboratory. Yearb Med Inform 2007;46 Suppl 1:138-40.
24. Schneider J. Telepathology at Tikur Anbessa Hospital: How telemedicine works. Ethiop Med J 2005;43:51-3.
25. Bianco M. Applications and end-user projects in Mediterranean countries: MedGeNet. EU-MED Conference. Brussels, Belgium: 23-24 October 2007.
26. Pagni F, Bono F, Di Bella C, Faravelli A, Cappellini A. Virtual surgical pathology in underdeveloped countries: The Zambia Project. Arch Pathol Lab Med 2011;135:215-9.