Shape Perception with Friction Model for Indirect Touch

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Abstract

The purpose of this paper is to study shape perception in the situation where the target object is interfered by other objects. This paper proposes a friction model that updates shear stiffness function of objects, in order to produce physics-based friction force in the situation of indirect touch. The result of experiments indicated that friction force influenced accuracy of indirect perception of convex shape.

1. Introduction

Touching an object in the situation, where the target object is interfered by other objects, occurs in many clinical occasions such as palpation. We call such a situation ***indirect touch.*** As shown in figure 1, palpation skill for specifying the place of tumors in the organ is especially important.

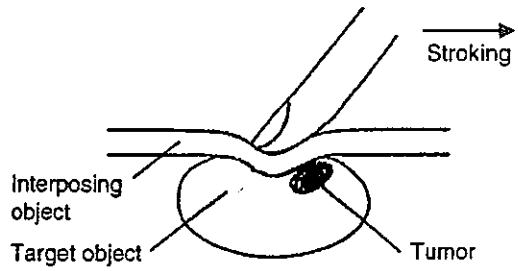

Figure 1. Shape perception in indirect touch

It requires indirect perception of both stiffness and shape information. Our study has simulated indirect stiffness perception [1]. Although Lederman et al. examined influence of spatially distributed forces on the fingertip on shape perception [2], few researches for the simulation of indirect shape perception have been found.

Robles-De-La-Torre et al. reported that force along stroking direction was important in perceiving concave and convex shape [3]. The authors applied the results on the case of indirect touch. Then, friction force, which is the force along stroking direction, will influence on shape perception. Foregoing friction models [4] were not applicable to the case, because collisions of soft tissues have not been considered.

This paper proposes friction model for indirect touch and examines influence of friction force on indirect shape perception.

2. Friction model for indirect touch

Friction model should simulate Coulomb friction force proportional to normal force. The important point is that the relation between force and displacement changes in indirect touch because of collisions of soft tissues. For stability of force feedback with interactive manipulation, the model is based on constrained-based method [5]. The amount of proxy movement Δu is given by

$$state = \begin{cases} sticking & (state = sticking, f_h < \mu_s f_n) \\ sliding & (state = sticking, f_h \geq \mu_s f_n) \\ sticking & (state = sliding, f_h < \varepsilon) \\ sliding & (state = sliding, f_h \geq \varepsilon) \end{cases} \quad (1)$$

$$\Delta u = \begin{cases} 0 & (state = sticking) \\ \overline{P_1 P_2'} - g^{-1}(\mu_d f_n) & (state = sliding) \end{cases} \quad (2)$$

where f_h and f_n are shear and normal force, P_1 is previous proxy position, P_2' is projected fingertip position onto surface polygon, g is a function of

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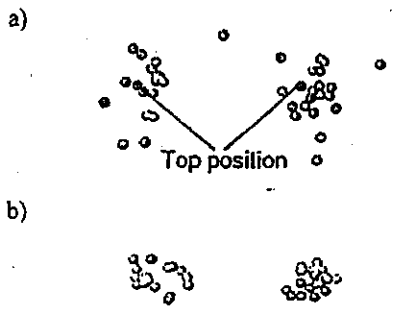
shear stiffness, μ_s and μ_d are coefficients of static and kinetic friction respectively, is a constant. Function g is repeatedly updated based on the values of shear force and displacement in the last clock period. The model enables to display stable friction force proportional to normal force.

3. Evaluation and results

Influence of friction force on indirect shape perception was examined. The experiment compared the case of applying proposed friction force with the case of applying no friction force [5].

Figure 2 shows simulation environments of experiments. Plate object (4745 tetrahedra) is located above sphere objects (5320 tetrahedra). All virtual objects have 1.0MPa elastic modulus and 0.4 Poisson ratios. Interaction between them is calculated with interaction model based on finite element method [1]. μ_s and μ_d are set as 0.0, 0.4 respectively. The simulator consists of PC (Dual CPU Xeon 2.8GHz) and PHANToM™.

gure 2. Simulation environments



ure 3. Results of indirect shape perception
Applying no friction [5] (Score: 0.37)
Applying friction by proposed model (Score: 0.27)

Five volunteers participated in the experiment. Each examinee tried to find top of sphere objects by stroking from upper side of plate object. Four trials are performed per each sphere object. The scores were calculated as the distance between the pointed and top position divided by a radius of the sphere objects. Pointed positions are plotted on the image of top view (Figure 3).

Fig. 3 showed decrease of the error of indirect perception by applying friction force. The average scores were 0.37 and 0.27, respectively. The statistical difference between the cases existed ($n=40$, $p<0.05$). The results of experiments showed that physics-based friction force was closely related to indirect shape perception.

4. Conclusion

This paper proposed physics-based friction model for indirect touch based on updating stiffness function and found the influence of friction force on indirect shape perception. Comparison with the case in real world and the study of correlation between finger movement and accuracy of perception is future works.

Acknowledgement

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References

[1] Y. Kuroda, M. Nakao, T. Kuroda, H. Oyama, M. Komori and T. Matsuda, "Interaction Model between Elastic Objects for Accurate Haptic Display", *Proc. of 13th ICAT*, pp.148-153, 2003

[2] S. J. Lederman and R. L. Klatzky, "Sensing and Displaying Spatially Distributed Fingertip Forces in Haptic Interfaces for Teleoperator and Virtual Environment Systems", *MIT PRESENCE*, Vol.8, No.1, pp.86-103, 1999

[3] G. Robles-De-La-Torre and V. Hayward, "Force Can Overcome Object Geometry in the Perception of Shape through Active Touch", *Nature*, Vol.412, pp.445-448, 2001

[4] T. H. Massie and J. K. Salisbury, "The Phantom Haptic Interface: A Device for Probing Virtual Objects", *ASME Haptic Interfaces for Virtual Environment and Teleoperator System*, 1994

[5] C. B. Zilles and J. K. Salisbury, "A Constraint-based God-object Method for Haptic Display", *Proc. of IEE/RSJ International Conference on Intelligent Robots and Systems, Human Robot Interaction, and Cooperative Robots*, Vol.3, pp.146-151, 1995

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MVL: Medical VR Simulation Library

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Abstract. In the last ten years, medical VR techniques have much progress and many simulators have been developed for education, planning, rehearsal and so on. On the other hand, developing a simulator takes much more labor and cost. In this paper, we propose MVL: Medical Virtual reality simulation Library, which supports simulation of several significant medical manipulations considering multiple organ interaction. The result of developing simulators using MVL confirmed validity about variety and developing cost.

1. Introduction

Virtual reality (VR) based simulation with physics-based deformation and force feedback gives much capability of medical application for education, training, planning and a lot of purposes. However, for developing simulators, much time and efforts are required for developers to learn and implement basic physics and foregoing methods. The aim of our study is to support and promote developing medical VR simulators by reducing developing burden. In this paper, we propose a simulation library ***MVL: Medical Virtual reality simulation Library***, which enables easy development of simulators with several important medical manipulations considering organ-organ interaction.

2. MVL

The features of MVL are as follows.

1. Multiple medical manipulations and multiple organ interaction
2. High accurate and interactive deformation and force display
3. API for simulating medical manipulations

MVL supports simulations of several significant medical manipulations such as palpation, cutting, retracting, and pushing aside. Simulation of both palpation and combination of cutting, retracting, and pushing aside achieves a lot of educational and training environment in elementary diagnosis and surgical approaching procedures respectively [1,2]. Interaction model between elastic objects [1] and collision detection method for deformable model [3] enables to simulate indirect palpation and pushing aside con-

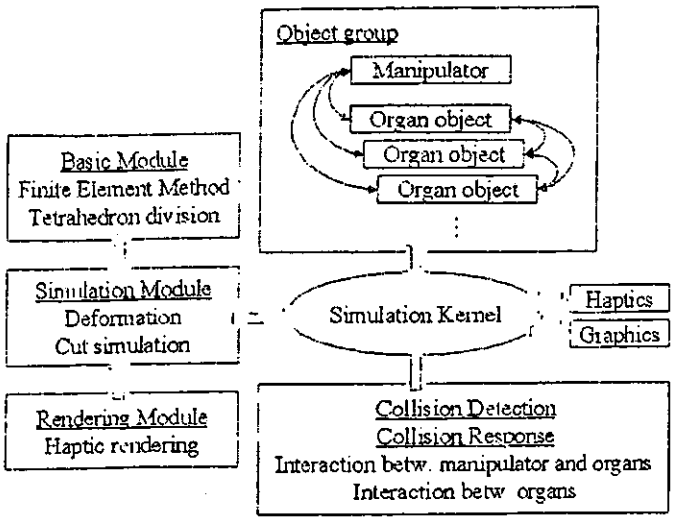


Figure 1. Architecture of MVL.

sidering behind objects. For high accurate deformation and force calculation, finite element method with condensation [4] and Hirota's methods [5] are implemented. API for medical manipulations is provided and enables simulation of medical manipulation with a few line coding.

Above features are achieved by *object group* based simulation architecture as shown in figure 1.

Object group class is an interface between users and simulation kernel. Just by adding a manipulator and organ objects into *object group* and a few line coding enables simulation of medical manipulations. All kinds of simulation modules including tetrahedron division, finite element method, haptic rendering, collision detection, organ interaction model are cooperated. Easy and flexible setting of physical parameters such as Young modulus and Poisson ratio are possible by using utility software called ***Matrix Builder***, which is provided by us.

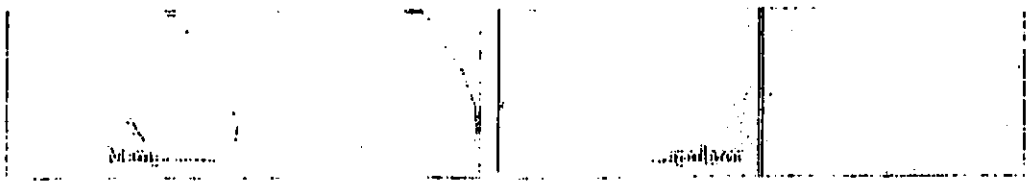
3. Results

Developed sample simulators using MVL and lines of coding are shown. Figure 2 and 3 show simulators of palpation and approaching thoracoabdominal aorta respectively [1,6].

The results confirm that MVL simulates various kinds of simulators and achieves reduced coding for developing simulators.

4. Conclusion

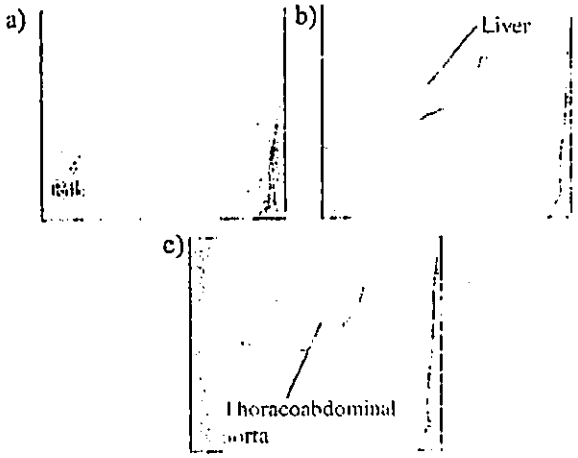
This paper proposes MVL, which is a supporting environment for developing force reflecting physics-based simulators. Object group based architecture manages all kinds of modules and provides API for simulating medical manipulations. The results confirmed that MVL simulates various kinds of simulators and achieves reduced coding for developing simulators. Japanese version of MVL is now available on the web site. Further development will be continued for advanced simulations.



```
1   // Initial setting:
2     MVLManipulatorObject* manipulator;
3     MVLElementObject *object1;
4     MVLObjectGroup* objGr;
5     manipulator = NewManipulatorObject();
6     object1 = NewElementObject();
7     object1->ReadObjectFile("aorta.fem");
8     objGr = NewObjectGroup();
9     objGr->AddManipulatorObject(manipulator);
10    objGr->AddObject(object1);
11    manipulator->SetPosition(SbVector(0.0f,0.0f,0.0f));
12    objGr->StartSimulation();
13  // Every time step:
14    manipulator->SetPosition(finger_pos);
```

```
1   // Initial setting:
2     MVLManipulatorObject* manipulator;
3     MVLElementObject *object1, *object2;
4     MVLObjectGroup* objGr;
5     manipulator = NewManipulatorObject();
6     object1 = NewElementObject();
7     object2 = NewElementObject();
8     object1->ReadObjectFile("rectum.fem");
9     object2->ReadObjectFile("prostate.fem");
10    objGr = NewObjectGroup();
11    objGr->AddManipulatorObject(manipulator);
12    objGr->AddObject(object1);
13    objGr->AddObject(object2);
14    manipulator->SetPosition(SbVector(0.0f,0.0f,0.0f));
15    objGr->StartSimulation();
16  // Every time step:
17    manipulator->SetPosition(finger_pos);
```

Figure 2. Palpation simulators Aorta palpation simulator (Left), rectal palpation simulator (Right) Each simulator is characterized as direct and indirect palpation respectively. Haptic display considering multiple organ interaction is achieved automatically just by difference in coding of registered number of objects.




```
1   // Initial setting:
2     MVLManipulatorObject* manipulator;
3     MVLElementObject **object;
4     MVLElementObject *object[10];
5     MVLCutElementObject *cutObject;
6     MVLObjectGroup* objGr;
7     manipulator = NewManipulatorObject();
8     objGr = NewObjectGroup();
9     cutObject = NewCutElementObject();
10    objGr->AddManipulatorObject(manipulator);
11    for(i=0;i<10;i++){
12      object[i] = NewElementObject();
13      object[i]->ReadObjectFile(organList[i]);
14      objGr->AddObject(object[i]);
15    }
16    manipulator->SetPosition(SbVector(0.0f,0.0f,0.0f));
17    objGr->StartSimulation();
18  // Every time step:
19    manipulator->SetPosition(finger_pos);
20  // Event:
21    cutObject-> CalculateCut(start_coord, end_coord, cut_vec);
22    cutObject->CalculateRetract(retract_value);
```

Figure 3. Approaching simulators Multiple surgical manipulations are conducted when approaching thoracoabdominal aorta. MVL supports development of a simulator dealing with several surgical manipulations. a) Before cutting between ribs. b) After retracting incision, liver covers a surgical field. c) Aorta is visible by pushing aside several surrounding organs.

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References

[1] Y. Kuroda, M. Nakao, T. Kuroda, H. Oyama, M. Komori and T. Matsuda, "FEM-Based Interaction Model Between Elastic Objects for Indirect Palpation Simulator", Proceedings of 12th Medicine Meets Virtual Reality Conference, pp.183-189, 2004.

[2] M. Nakao, T. Kuroda, H. Oyama, M. Komori, T. Matsuda and T. Takahashi, "Planning and Training of Minimally Invasive Surgery by Integrating Soft Tissue Cuts with Surgical Views Reproduction", Computer Assisted Radiology and Surgery(CARS), pp. 13-18, 2002.
[3] Y. Kitamura, A. Smith, H. Takemura and F. Kishino, "A Real-Time Algorithm for Accurate Collision Detection for Deformable Polyhedral Objects", MIT PRESENCE, Vol.7, No.1, pp.36-52, 1998.
[4] M. Bro-Nielsen, "Finite element modeling in surgery simulation", Journal of the IEEE. Vol.86, No.3, pp.490-503, 1998.
[5] K. Hirota and T. Kaneko, "A method of representing soft object in virtual environment", IPSJ JOURNAL, Vol.39, No.12, pp.3261-3268, Dec. 1998
[6] M. Nakao, T Kuroda, M. Komori and H. Oyama, "Evaluation and User Study of Haptic Simulator for Learning Palpation in Cardiovascular Surgery", International Conference of Artificial Reality and Tele-Existence, pp.203-208, 2003.

原著

共有VR型手術シミュレータの医学体験教育への適用

黒田知宏[1)]，原田雅之[2)]，寺田尚史[3)]，小山博史[4)]

近年の医学を取り巻く状況が厳しくなっていることを反映し，中高校生の医学志望者の減少と，一般社会における医学教育への社会的理解の低下が問題となってきている。ある事象の社会的理解を高めるためには，具体的な例を取り上げ，専門家の指導を得ながら体験させることが最も効果的であると考えられるが，医療分野においては，体験環境の提供と教育に当たる専門家の確保が困難である。

本論文では，ネットワークを介して仮想の術野を共有する共有VR型手術シミュレータを開発した。本シミュレータを適用することで，医師に移動の負荷をかけることなく，誰でも医師の指導下での外科手術の体験が可能になる。本シミュレータを用いた遠隔指導下での仮想手術体験学習実験を行ったところ，被験者の医学・手術に対する興味の向上が確認された。

1. はじめに

近年の大学入学年齢層人口の減少と，近年の相次ぐ新設大学の設置によって，進学競争率は低下の一途にある。これに伴い，1990年前半の第2次ベビーブーム世代入学時には，高競争率を誇った医学部の競争率も徐々に低下傾向を示している。一方で，長

Applying Shared-VR based Surgical Simulator for Medical Trial Study

Tomohiro KURODA, Masayuki HARADA, Takafumi TERADA, Hiroshi OYAMA

Abstract :

This paper describes a surgical simulator based on shared virtual reality technique. The simulator enables users to share virtual surgical fields over information network and to perform collaborative virtual surgery within the shared virtual space. Thus, the simulator lets any person to experience surgical simulation under the guidance of expert doctors. Consequently, the simulator may promote social understandings for clinical and surgical works. The simulator evaluated under distributed surgical training for high school students and the results indicate that an experience under the developed simulator promotes interests about the clinical and surgical works.

Key words :

Shared Virtual Reality, Surgical Simulator, Introduction Study

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い間の受験戦争の加熱により，医学部の「ブランド化」が進み，必ずしも医師を志していない学生に，偏差値が高いことだけを理由に医学部受験を勧める教育が一部教育機関で行われることにより，医師としての職業意識の低い医学生が増加する問題が発生している。

一方，近年医療事故に対する社会的注目の高まりから，やや過熱気味の医療事故報道が行われ，外科医として生きることのリスクがにわかにクローズアップされている。80年代以降，外科医数の伸び悩みや外科医の不足が指摘されている[1]が，上述の社会的リスクへの注目や外科医の労働環境の悪化，さらには上述の医学生の気質変化に伴って，外科医の志望者数の減少が顕著となっている。外科医数の減少はわが国が高水準な医療を維持するうえで深刻な問題である。

一方，第16期中央教育審議会から「心の教育」を重視する答申が示されたことを受け，全国の小中学校では様々な「社会体験学習」が実施されている。体験学習は，生徒の勤労観，自己効力感，社会指向性等を高め，社会的発達を促進する[2]とともに，農業や町工場での実習が，これらの業種への関心を高める効果があることが明らかにされている[3][4]。

したがって，医療に対する社会的理解を高め，医療者を志す学生を早期に育成するためには，医療分野において，体験教育を導入することが効果的であると考えられる。しかし，医療分野においては，専門家の直接の指導を受けながら実際の業務を体験することのできる環境を中高生に提供することは非常に困難である。

本研究では，互いに離れた空間にいる二者がネットワークを介して仮想術野空間を共有し，仮想術具を用いた協調作業を行うことができる共有VR型手術シミュレータを適用することで，上記の問題を解消することを提案し，その有効性を検証する。

2. 医用VRシステムの教育応用

これまでに，基礎医学教育[5]，手術リハーサル[6]，画像診断[7]など様々な用途の医用VRシステムが開発されているが，特に手術手技教育は重要な応用例としてとらえられている。中でもカメラ画像下で術具を用いて術野を操作する内視鏡術は，VRとの整合性が高いことから，様々な内視鏡下訓練シミュレータが開発されている[8,9]。

一方で，教育用VRシステムの教育効果についての検討や技能検定の試みはそれほど多くない[10]。筆者らは顕微鏡下眼科手術シミュレータ[11]を用いて医学部5回生を対象とした手技技能分析の試みを行い，手技実施時間と出血点数の間に一定の関係を認めた[12]。同実験では，臨床実習において仮想手技体験を行うことで，自らの「器用さ」を体験し，学生が進路決定の判断材料とする例がみられるなど，一定の教育的効果が認められている。しかし，医用VRを非医療者の体験学習に適用した例は，筆者らの知る限り存在しない。

3. 仮想空間の共有技術

ネットワークを介して仮想空間を共有する分散仮想環境（Distributed Virtual Environment：DVE）[13]構築の試みは，80年代の戦略シミュレータ[14]や協調デザイン環境[15]の開発を皮切りに，様々な分野で研究が行われ，複数のツールキットが提供されるに至っている[16]~[18]。

医療分野においては，術中のナビゲーションや遠隔手術などへの適用が考えられる。筆者らも，遠隔地から術野内へプロジェクタ型協調現実感環境を用いて指示を提供する共有MR空間型遠隔医療支援システムを構築し，空間情報の指示において時間短縮効果をあげられることを確認した[19]。

共有仮想空間構築においては，複数の仮想空間を同一の状態に保つ一貫性制御が重要な役割を果たす[20]。一貫性制御においては，インタラクション性を減じることなく，複数サイトで行われた異なる操作を反映することが必要であり，並列アルゴリズム

で用いられる操作オブジェクトに対する事前ロック取得手法などの適用は好ましくない。一方で，複数サイトでの操作のうち，ある1サイトだけの操作を受理する手法も提案されているが，対象となるオブジェクトが複数サイトの操作を交互に反映することによるジャンプ現象などが報告されている[14]。筆者らは複数の操作を一端「選択候補」として受け入れておき，1つ以上を選択させる「複製－選択プロトコル」を提案している[20]が，医用VRのようにリアルタイムで操作が反映されねばならない仮想環境には適さない。

4. 共有VR型手術シミュレータ

4.1 空間共有手法

本研究では，脳神経外科手術シミュレータ[21]をネットワーク接続し，複数のサイトから術野に介入することができる共有VR型手術シミュレータを構築した。

3.で述べたとおり，一貫性制御は共有仮想空間構築において重要な課題である。特に，手術シミュレータでは視覚情報だけでなく，術具と組織の干渉によって発生する力覚情報の提供が重要であり，1,000 Hzの更新レートが必要とされる[22]力覚情報について，適切な一貫性制御が必要となる。しかし，物理的に妥当性のある反力提示を可能とする有限要素法に基づいた反力算出のためには，巨大な有限要素マトリックスを把持する必要があり，かつ，有限要素マトリックスは術具と組織の干渉状態によって大きく変化するため，干渉状態が変わるたびに巨大なマトリックスをサイト間で送信する必要がある。また，有限要素マトリックスの算出には術具の位置情報が必要であり，全クライアントで同じ反力提示を行うためには，力覚計算前に術具位置情報の一貫性が保たれていることを保証する必要がある。したがって，空間を共有するサイトに演算速度や通信速度が遅いPCが含まれる場合には，全体のパフォーマンスを落としてしまうこととなる。

以上より，構築システムは1台のサーバ上で，それまでに受信した術具位置の情報をもとに，変形・反力計算を行い，変形後の組織形状データと術具への反力データをクライアント機に送信するサーバ＝クライアント構成とした。これにより，一貫性制御の問題を回避するとともに，通信量の削減を図っている。なお，送付する形状データを組織内の変形しうる血管部位のみに限定することで，更なる通信量削減を図っている。

4.2 性能測定実験

4.1で述べた方法を適用した際の更新レートおよび通信量の測定を行った。実験は，表1に示すスペックのPCを100 Base－TX対応のスイッチングハブを介して直結して実施した。計測条件および計測結果を表2に示す。ただし，力覚更新レートは力覚付術具装置がPC1のみに装着されていたため，PC1上での更新レートを示している。また，通信量は更新レートの中間値に対するアプリケーションレベルでの通信量であり，TCP/IP通信時に付加されるヘッダや制御パケットの量を含まない。

結果から，構築システムは，汎用PCと汎用ネットワーク回線上で十分な更新レートを実現できることが明らかになった。

5. 遠隔体験学習実験

5.1 実験方法

4.で構築したシステムを体験教育に適用する実験

表1 計測PCのスペック

	PC－1	PC－2
CPU	P－III 866 MHz Dual	P－III 2.4 GHz Dual
メモリ	512 MB	1 GB
映像	WildcatPro	RADEON 9700 Pro
デバイス	6自由度（力覚付）	4自由度（力覚無）
OS	Windows NT 4	Windows 2000

表2 通信量計測結果

実験番号	1	2	3	4	5	6
可動部接点数（点）	164	164	80	80	164	164
テクスチャの有無	有	有	有	有	無	無
サーバとしたPC	PC－2	PC－1	PC－2	PC－1	PC－2	PC－1
PC1映像更新レート（Hz）	50－60	30－45	50－60	53－55	50－60	30－45
PC2映像更新レート（Hz）	65－70	40－100	80－90	50－100	65－70	30－45
力覚更新レート（Hz）	700－1000	2550－2670	1450－1550	2400－2600	950－1300	270－3000
映像通信データ量（Kbyte/sec）	86	109	86	117	86	109
力覚通信データ量（Kbyte/sec）	184		302		243	
総通信量（Kbyte/sec）	270	109	388	117	329	109

を行った。2003年8月12日に京都大学で行われたオープンキャンパスにおいて，事前予約によって選ばれた工学部見学者17名を対象に，構築シミュレータを用いた遠隔手術体験実習を行い，体験前後の興味の変化をアンケートによって調査した。

実験では，図1に示すように，京都大学大学院情報学研究科医用工学研究室に設置した生徒用端末と京都大学医学部附属病院開発室に設置した教師用端末を，京都大学学内LAN網（KUINS－Ⅲ）内に確保した専用VLANを用いて接続し，共有VR手術環境を構築した。また，教師と生徒間にはMicrosoft NetMeetingを用いたテレビ電話回線を設置した。なお，KUINS－Ⅲは，フロアルータ間を結ぶ基幹回線がギガビットで構築され，フロアルータの各ポートが各教室の情報コンセントに直結され，100Base－TXの接続環境を提供するローカルギガビットネットワークである。

実験では，情報学研究科を訪れた見学者に対して，まずアンケート調査を実施して事前の興味を確かめた後，医用VRシミュレータについて同研究室のスタッフが説明を行いながら仮想手術を実演した。続いて見学者は，附属病院側の脳神経外科研修医の介助を受けながら，仮想手術を体験する。体験手技は脳幹部脳動脈瘤クリップ術とし，教師が左手

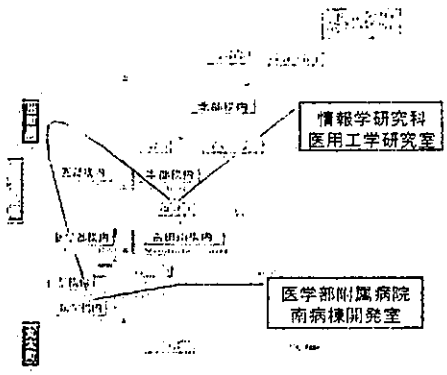

図1 実験ネットワーク構成

に把持したへらによる介助を受けながら，見学者は右手に把持したクリップを動脈瘤にかける手技を行った。なお，見学時間の関係上，実際に手技を行ったのは，3班の見学グループそれぞれにつき，希望した1名のみとした。実技終了後，あらためて同じアンケートを実施し，興味の変化を調査した。

アンケートでは，情報学・医学・手術・VRに対する興味の有無を，5分点スケール上に記載してもらった。また，体験後の感想を自由に記載してもらった。

表3 通信量計測結果

		基本情報		情報			VR			医学			手術		
		年齢	体験	前	後	増分	前	後	増分	前	後	増分	前	後	増分
見学1		15	無	5.0	5.0	0.0	4.0	5.0	1.0	4.0	4.0	0.0	3.0	4.0	1.0
		16	無	4.0	5.0	1.0	5.0	5.0	0.0	5.0	5.0	0.0	5.0	5.0	0.0
		18	無	2.0	2.0	0.0	2.0	2.0	0.0	3.0	3.0	0.0	3.0	2.0	-1.0
		17	無	4.0	4.0	0.0	5.0	5.0	0.0	3.0	4.0	1.0	3.0	4.0	1.0
見学2		18	有	5.0	5.0	0.0	5.0	5.0	0.0	5.0	5.0	0.0	5.0	5.0	0.0
		16	無	4.0	4.0	0.0	4.0	4.0	0.0	2.0	2.0	0.0	2.0	2.0	0.0
		16	無	4.0	4.0	0.0	4.0	5.0	1.0	4.0	4.0	0.0	3.0	4.0	1.0
		16	無	4.0	5.0	1.0	4.0	4.0	0.0	3.0	3.0	0.0	2.0	2.0	0.0
		18	有	5.0	5.0	0.0	5.0	5.0	0.0	5.0	5.0	0.0	5.0	5.0	0.0
		17	無	5.0	5.0	0.0	2.0	3.0	1.0	2.0	3.0	1.0	2.0	3.0	1.0
見学3		16	無	1.0	1.0	0.0	3.0	4.0	1.0	1.0	2.0	1.0	3.0	3.0	0.0
		19	有	5.0	5.0	0.0	5.0	5.0	0.0	4.0	5.0	1.0	4.0	5.0	1.0
		19	無	4.0	4.0	0.0	5.0	5.0	0.0	3.0	3.0	0.0	2.0	3.0	1.0
		15	無	2.0	2.0	0.0	2.0	4.0	2.0	3.0	3.0	0.0	3.0	3.0	0.0
平均	全体	16.9		3.9	4.0	0.1	3.9	4.4	0.4	3.4	3.6	0.3	3.2	3.6	0.4
	体験有			5.0	5.0	0.0	5.0	5.0	0.0	4.7	5.0	0.3	4.7	5.0	0.3
	体験無			3.6	3.8	0.2	3.7	4.2	0.5	3.1	3.4	0.3	2.9	3.3	0.4

5.2 結果と考察

一部の評価点が記載されていなかった3名を除いた14名について，集計結果を表3に示す。なお，得点は1～5点の幅で，得点が高いほど興味が高いことを示している。実験結果より，体験学習前後において，興味が増加する傾向がみられた。

まず体験者と非体験者（見学者）について調査したところ，非体験者について顕著な興味の増加がみられた。体験者は「体験希望者」であり，体験前から高い興味を持っていたため，大きく変化しなかったことが結果より読み取れる。

被験者は全員が工学部志望者であり，情報学・VRの2分野の得点は体験前より高い値を示している。一方で，医学・手術といった分野については，中央値付近からやや高い値に変化しており，体験者の興味を引くことに成功していることがわかる。

実験後の感想では，「医学に興味が沸いた」「仮想手術で手術をより確実にしたい」等の肯定的，かつ主体的に関わる意欲を持った解答がいくつかみられ，被験者の医学・医用工学への興味が高まったことがみてとれる。

一方，実験に参加した研修医からも「おもしろい」という意見があり，指導側にも一定の効果があったことがみてとれた。地域体験学習などにおいて指導者側にも，生徒や地域との関わり方において好ましい効果を発揮することが指摘されており[23]，本実験でも同様の効果があったものと考えられる。

6. 終わりに

本研究では，共有VR型仮想手術シミュレータを構築し，これを体験学習に適用することを試みた。共有VR型仮想手術シミュレータを用いることで，通常体験させることが困難な医療体験を，遠隔地の医療従事者の指導のもとで体験させることができる。また，遠隔体験教育実験より，仮想体験教育を通じて学生の医学に対する興味を向上することができることが明らかになった。今後，医用VRシステムが医学生への教育だけでなく，社会に医学への理解を広げるための1つの道具として，広く適用されることを期待する。

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文献

1) 吉井一匡：特集外科医の明日―迫られる現状打破―. 民間医局 2003；40：11-20
2) 志村昌之，土井進：農作業における子どもの「体験」と「学び」を結ぶ支援－「信大YOU遊プラザ」に見る学生の実践－. 信州大学教育学部附属教育実践総合センター紀要 2002；3：97-106
3) 小林宏：中学生の「社会体験学習」の効果に関する研究. 兵庫県立教育研修所研究紀要 1999；110
4) 浅野志保：小学校の農作業体験学習とその効果練馬区を事例として. 卒業論文，千葉大学園芸経済学科 2002；
5) Hohne K.H.(ed)：Voxel-Man, Springer-Verlag Electric Media 1995；
6) 中尾恵，黒田知宏，小山博史他：組織切開・開創シミュレーションによる手術計画支援. 日本バーチャルリアリティ学会論文誌 2003；8(2)：163-170
7) 鳥脇純一郎：Virtual Endoscopyと外科応用. 手術 2000；54(12)：1817-1823
8) Kuhnapfel U, Cakmak H.K, Mass H：Endoscopic Surgery Training Using Virtual Reality and Deformable Tissue Simulation. Computers & Graphics 2000；24(5)：671-682
9) 向井信彦，原田雅之，小山博史：リアルタイム手術シミュレータの構築. VR医学 2002；1(1)：72-77
10) 小山博史：Virtual Reality技術を用いた新しい手術教育. VR医学 2002；1(1)：30-39
11) 向井信彦，原田雅之，室井克信他：PCベースリアルタイム手術シミュレータの開発. 電子情報通信学会論文誌 2001；J 84-D-II(6)：1213-1221
12) Oyama H, Kuroda T, Hori K et al：Efficiency of a Virtual Reality Simulator for Evaluating the Aptitude of Medical Students. General Medicine 2001；2(1)：17-23
13) Singhal S, Zyda M(ed)：Networked Virtual Environments Design and Implementation, Addison Wesley 2000；
14) Calvin J. et al：The SIMNET Virtual World Architecture. Proceedings of the IEEE VRAIS'931993；450-455
15) 竹村治雄，岸野文郎：臨場感通信会議と仮想空間操作. 映像研究特別論文集 CG'921992；188-193
16) Shaw C, Green M：The MR toolkit peers package and Experiment. Proceedings of IEEE VRAIS'931993；18-22
17) Frecon E, Stenius M：DVAE：A Scalable Network Architecture for Distributed Virtual Environments, Distributed Systems Engineering Journal 1998；5(3)：91-100
18) Leigh J, Defanti T.A：CAVERN：A Distributed Architecture for Supporting Scalable Persistence and Interoperability in Collaborative Virtual Environments. Virtual Reality：Research, Development and Applications 1996；2.2：217-237
19) 末永貴俊，飯野恵秋，黒田知宏他：遠隔超音波画像診断におけるプローブ操作教示システム. 電子情報通信学会論文誌 2000；J 83-D-II(1,)：324-334
20) 南広一，Tomi Korpipaa，黒田知宏他：分散デザイン作業支援のための空間管理手法. ヒューマンインタフェース学会論文誌 2002；4(3)159-165
21) 原田雅之，向井信彦，小山博史：脳神経外科種鬱シミュレータにおける動脈モデル. VR医学 2002；1(1)16-20
22) Komori M, Yoshida R, Matsuda T et al.：User Haptic Characteristics Measurement for Design of Medical VR Applications. Proceedings of Computer Assisted Radiology and Surgery 2000；17-22
23) 宮地孝宣：地域組織主導の「勤労体験学習」の実践と効果. 国立オリンピック祈念青少年総合センター紀要 2003；3：225-232

UMLSを利用した日本語医学知識サポートシステム

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Knowledge support system for medical information retrieval in Japanese using UMLS Metathesaurus

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Abstract: Japanese medical terms are already mapped to UMLS (MeSH), and we can use Japanese term to search articles in MEDLINE. When medical students search MEDLINE, there may arise terms whose sense are unknown for them. Same situations occur when physicians search something not in their field, or ordinary people search articles in MEDLINE. Here any knowledge support system for unknown terms may be usuful in these cases. Using UMLS semantic network, SNOMED-CT, and UMLS MRCOC resources, we developed interfaces for people to find a word sence within a systematic knowledge.

Keywords: UMLS, SNOMED-CT, information retrieval, knowledge support

1. 背景

医学生がMEDLINEを検索する場合、医者が自分の専門外の領域を検索する場合、さらには一般の人々がMEDLINEを検索する場合、こうした場面で「検索語が何を意味する語彙なのかわからない」または「検索によって得られた語彙が何を意味するのかわからない」といった事態が生じているのではないだろうか。こんな時、かつては医学書や百科事典を調べていた。調べたい項目が載っている本を探すことから始まり、索引を使って何項目かを読んで理解したものである。最近ではgoogleなどインターネット検索エンジンを利用してリストされたサイトに行き、そこに書かれていることをいくつか読めば、おおよその意味は理解できる。

いずれの場合も、その語彙に関する記述は、体系的知識とトピックスという2つに分けることができる。体系的とは何らかの知識体系の中での位置づけを述べたもの、トピックスとはその語彙に関する、より専門的な研究などを指す。例えばプロラクチンは下垂体前葉から分泌されるホルモンで、前葉ホルモンには他にTSH、ACTH、RHがある、というのが体系的知識。高プロラクチン血症の治療法、プロラクチン産生腫瘍の診断などがトピックスである。前者は解剖学、生理学など、教科書的な知識とも言い換えることができる。後者は断片的であるが最新の知識を記述し、その理解には前者の理解が前提となっている。

ここでは、ある語彙が「何を意味しているのか」を調べようとする際には、多くの場合、体系的知識を求めているものと仮定する。さて、こうした体系的知識は既存の統制用語集の中にすでに概念間関係として記述されているのではないだろうか。例えばUMLSのSemantic networkやSNOMED-CTの概念間関係記述などである。

これまでに、英語の医学用語の位置づけを示すサービスにはUMLSのSemantic Navigator[1]など、多くの意欲的な試みがあるが、日本語に関しては目立つものがなく、しかも検索に直結した知識支援は見あたらない。すでに日本語医学用語とMeSHとの対応付けによって[2]、日本語キーワードからMEDLINE検索を行うことができるようになっている。そこでこれにSNOMED-CTなどに含まれる医学知識を取り出して体系的知識として供給することによって、文献検索時に医学知識を支援する仕組みを構築することを考えた。

2. 目的

日本語によるMEDLINE(PubMed)検索時に、利用者が不明と思う医学用語に対し、その用語の体系的な医学知識を支援すること

3. 方法

3.1 材料

使用したUMLSのバージョンは2004ABし、SNOMED-CTはUMLSに包含されているものを利用。またMeSHに対応した日本語医学用語として、医学中央雑誌刊行会の医学用語シソーラス第5版を利用した。これらのリソースはLinux上のPostgreSQLに格納し、ユーザーインターフェイスはMacromedia Flashを利用して構築した。FlashとPostgresSQLとの間の接続にはphpを利用した。作成したインターフェイスを数名にテストしてもらい感想を得た。

3.2 日本語医学用語とUMLSとの対応付け

日本語医学用語は2004年版のUMLS MetathesaurusからMeSHに対応する日本語が含まれるようになった。また医学中央雑誌刊行会の医学用語シソーラス第5版はMeSHに対応している。そこでこの両者を使ってMeSHと日本語とのマッピ

ングを行った。MeSHの概念数は約2万であり、同義語も含めた語彙数はMeSH日本語版と医中誌を併せて104346とした。以上を利用して、調べたい語彙を同義語中に含む概念を検索し、その概念のリードタームをリストし、その中から調べたいものを選択することにした。

3.3 UMLSセマンティックネットワーク

これはUMLS概念を統一的な意味タイプ(189種)に分類してそれらの関係(49種)を記述したものである。UMLSの各概念は少なくともひとつの意味タイプに属する。ここでは、意味を調べたい語彙の属する概念が、どの意味タイプに属するかを提示し、その意味タイプからどのような関係がどこの意味タイプに出ているのか、を利用者に見せることにより、その言葉がどのような位置づけにあるのかを示唆する。

例えば胃癌は'Neoplastic process'という意味タイプに属する。この意味タイプから他の66種の意味タイプへ13種の関係が伸び、逆に他の88種の意味タイプから19種の関係が戻ってくる。これらの意味タイプと関係を見ることである程度の体系的知識を得ることが期待できる。しかし例えば胃癌と胃癌脳転移とはどちらも'Neoplastic process'なので、この概念間では何の関係も得られず、有効ではない。

3.4 SNOMED-CT

臨床用語のシソーラスであると同時に臨床概念間の関係を記述したオントロジーであり、語彙数は単独の統制用語集としては世界最大である。2004年からはUMLSに含まれるようになり、日本でも個別に米国病理学会(CAP)と契約を結べば利用することができる。日本語とMeSHとは対応が付いているので、UMLSを介してMeSH概念に一致するSNOMED概念があれば、日本語でSNOMED-CTの関係を利用することができる。

しかしSNOMED-CTで定義されている概念間関係は108万件。うちMeSHで記述できる関係数は2万件、うち日本語で記述できた概念間関係は16943件であった。これはSNOMED-CTの概念数がMeSHに比べてあまりに多いため、MeSHで記述できるSNOMEDの関係が非常に少なくなってしまうためである。実際、MeSHの概念数は2万、SNOMEDの概念数は30万、両者に共通する概念数は12000あまりに過ぎない。そこでSNOMED-CTでの概念名と関係を示した上に、日本語で表示できるものがあれば置換する、という方式にした。例えば胃癌の親概念は胃疾患、腹腔臓器腫瘍、消化器腫瘍、子概念は噴門部腫瘍、大弯部腫瘍、幽門腫瘍など、その他の関係として所見のある場所が胃である、家族歴に胃癌を伴う、などが定義されている。これらのうち、子概念のすべて、および家族歴に関する記述などは対応する日本語が存在しない。しかし英語としてSNOMED-CTの記述を併せて見ることによって、もとの概念の体系的知識に対する位置づけを把握することができた。

3.5 MRCOC

UMLSには、MEDLINEの文献中でひとつの文献に付されているMeSHの主キーワードが共起する頻度が収められている。例えば高血圧には降圧剤、血圧、ACE阻害剤などが高頻度に現れる。これらの概念はもとの高血圧という概念に対して何らかの関連を有しており、その関連性を体系的知識の中に位置づけることができれば有用と考えられる。ここでは、不明な語彙に対してMRCOCで関連性が高い概念を頻度順に提示し、このリストの中から概念を選択すると、元の語彙と併せて、両者がSemantic NetworkあるいはSNOMED-CT上でどのような関連にあるのかを提示する仕組みを作った。

実はこのMRCOCによる情報を使うと、元の概念に対して他のどのような概念が研究論文の中に頻出するか、という観点から検索を行うことができるため、それ自体が有用なツールである。しかしこれを不明な語彙に対して適用すると、その不明な語彙と関連の高い順に、出現した既知の語彙との関連性から元の語彙の意味を推し量る、という使い方になるため、毎度SNOMED-CTやSemantic Networkによる語彙間の関連性を参照しなくてはならず、面倒である。不明な語彙の意味的な位置づけを探すのであれば、SNOMED-CTでの位置づけを見る方が有用であった。

4. 結果

以上の方法に従い、文献検索を行う際に疑問を持った語彙に対して、知識支援を行うインターフェイスを構築した。医師が使用した場合には、体系的な位置づけを見るのにはかなり有効であるとの感想を得た。しかし医学以外を専門とする学生の場合には、体系的な知識そのものの理解が難しく、有用かもしれないという程度の感想に留まった。一般の人々に医学知識を平易に伝えるにはまだ一工夫必要であるが、ある程度の医学知識のある者には有用と思われる。

参考文献

[1] http://umlsks.nlm.nih.gov/

[2] Yuzo Onogi et. al. Mapping Japanese Medical Terms to UMLS Metathesaurus. Proceedings of the 11th World Congress on Medical Informatics, pp. 406-410, 2004.

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Amsterdam: IOS Press

Mapping Japanese Medical Terms to UMLS Metathesaurus

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Abstract

This paper introduces and reports the results for a project to map Japanese medical terms to the UMLS Metathesaurus. The "Thesaurus for Medical and Health related Terms version 5" published in 2003 by the Japan Medical Abstracts Society and UMLS version 2002AC provided by NLM were used in this study. The goal was to judge the validity of the correlation between the Japanese and English terms that belong to the same MeSH concept. Fifteen medicine, nursing, and library science professionals, excluding JAMAS, used a custom designed Web interface to perform this task. About 10% of the concepts were judged as invalid, and the reasoning behind these failures were analyzed. Experience from this project can be used to estimate the manpower required to revise the Japanese thesaurus after future revisions to UMLS or MeSH.

Keywords

UMLS, MeSH, Japanese Medical Terms

Introduction

In order to accurately exchange information, it is imperative that concepts and terms have universal meanings. This is the motivation behind the development and maintenance of standard health terminologies and controlled vocabularies. The Unified Medical Language System (UMLS) project was initiated in 1986 by the U.S. National Library of Medicine to integrate these controlled vocabularies [1]. The UMLS Knowledge Sources, which now provides valuable information about biomedical concepts, incorporates tools to accomplish searches on the root terms used to name the concepts [2,3].

However, information exchange is much more difficult in a multilingual environment [4,5]. Although the UMLS currently contributes to cross-language retrieval by supporting terms in 15 languages, Japanese vocabulary is excluded. There is a great need for Japanese professionals to enter queries in Japanese and retrieve documents, even if they are written in English. Currently, professionals typically use MEDLINE via Ovid technologies, Inc. or PubMed services provided by NLM. A set of Japanese biomedical terms that correspond to or closely relate to MeSH or UMLS concepts is needed in order to search articles in Medline using Japanese keywords.

Only a few controlled vocabularies have been developed and maintained in Japan. The primary interest of the Japanese medical society has instead been focused on nomenclature alone, without semantic structure, in order to coordinate with the English representation. This might have originated from difficulty inputting kanji characters using the keyboard, which delayed the establishment of health information databases. And Japanese terms are written using more than 2000 Kanji characters, 83 Hiragana characters, and 96 Katakana characters. Most terms of foreign origin are written using Katakana, which is a phonetic alphabet. However, when there are variations in pronunciation for a foreign term, a number of Katakana variations exist for a single term. This characteristic is prominent in medical terms that originate from personal names. Hiragana is also phonetic, however it is primarily used to detail the pronunciation of the kanji character(s), when they appear in nouns. This feature of Japanese writing may be another reason why controlled vocabularies for Japanese medical and health-related terms have lagged.

In the information age, it is increasingly important for medical information specialists to collect, accumulate, and analyze health related information written in Japanese. This advancement is particularly important for electronic health records. This application has led to increasing research interest in developing controlled vocabularies in Japanese [6-8]. Now we do have a set of standard Japanese disease names corresponding to ICD10, but there are no vocabularies in regard to Japanese clinical terms.

In 2003, the Japan Medical Abstracts Society published the "Thesaurus for Medical and Health Related Terms, version 5." This Japanese thesaurus corresponded to MeSH, but were not checked in public, might not correspond to MeSH correctly, nor cover enough clinical terms used in practice.

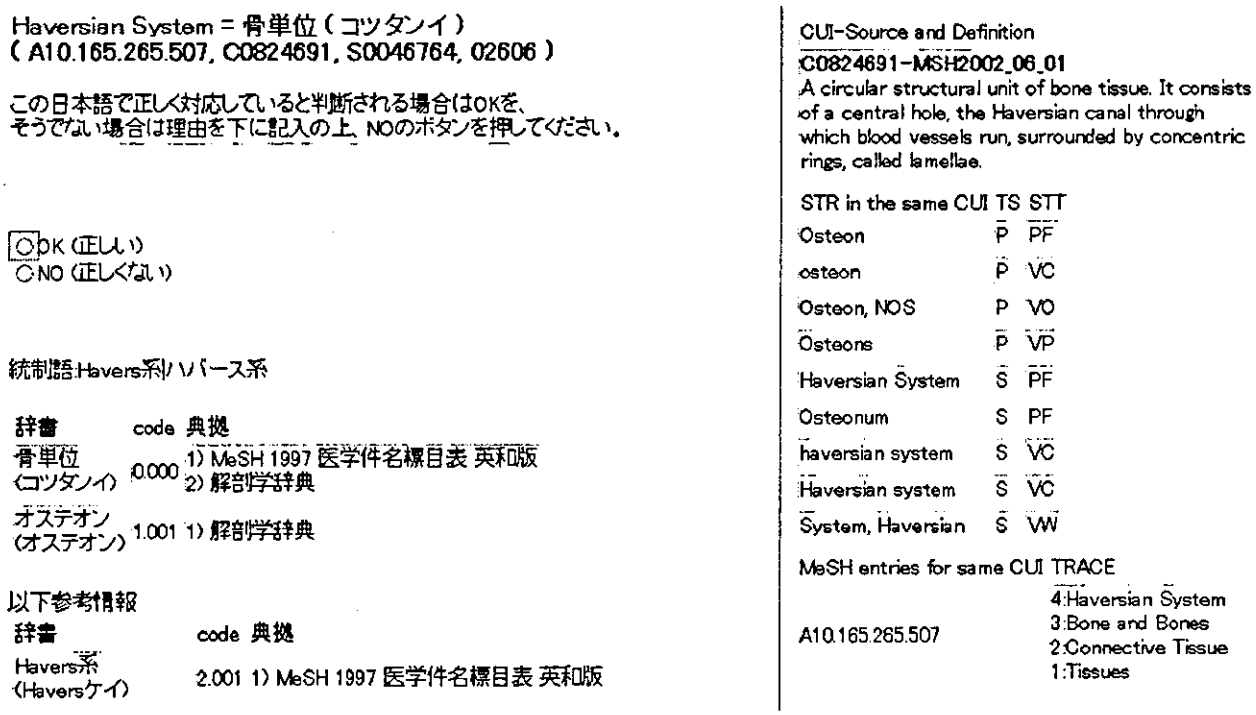

Figure 1 - User interface for verification of correspondence between a set of terms within a Japanese medical concept and English terms in the same UMLS concept. On the left, Japanese medical terms and their synonyms and sources are diplayed. On the right, the corresponding English terms for the same UMLS concept are displayed. The judging process is completed by pushing the «OK» or «NO» button in the upper left corner. When judged as «NO», the reasons for the judgment are required in the text box.

Therefore, a team of health-related professionals checked the validity of the Japanese terms in this thesaurus to determine if they properly correspond to their English counterparts based on both the indexers' and the health professionals' points of view. Terms that were judged poorly were discussed and either removed or replaced by other more appropriate Japanese medical terms. The purpose of this article is to describe the validation project and report its initial results.

Materials and Methods

Materials

The following resources were used to research the health-related terms:

1. UMLS version 2002AC, provided by NLM.
2. The "Thesaurus for Medical and Health Related Terms version 5," referred to as the TMH, was used as a collection of Japanese medical terms. The TMH was published in 2003 by the Japan Medical Abstracts Society (JAMAS).
3. The Database and WWW server for this system used Apache version 1.3.27 with php 4.2.3 module and PostgreSQL 7.2.3 DBMS, running on Red Hat Linux 7.3.

Concepts and strings that were related to MeSH were used from UMLS. There were 20,603 concepts (descriptors) and 37,864 MeSH entries used. The concepts numbered approximately half of the MeSH tree entries because some concepts have multiple entries. For example, the concept "Diabetes Mellitus" has two entries: MeSH tree numbers C19.246 and C18.452.297, and "WAGR Syndrome" has 18 MeSH numbers. However, many concepts only correspond to one MeSH tree number.

The TMH thesaurus contains 84,617 Japanese biomedical terms, which are categorized in 19,179 MeSH concepts, based on the MeSH 2001 version. Japanese indexers from the Japan Medical Abstracts Society extracted these terms from Japanese articles that were published in Japan. The indexers have also extracted additional terms that relate to each concept, resulting in a total of 95,071 terms.

Methods

Phase one involves checking the correlation between the Japanese terms and the UMLS strings for every UMLS concept within MeSH. More specifically, a web interface was used to repeatedly judge the correlation between a set of Japanese terms and a set of English strings for the same MeSH (UMLS) concept. During this process, concepts that had been changed from 2001 to 2002 were excluded. The MeSH terms that appeared more than once in the MeSH tree were judged multiple times. If there were multiple judgments for one set of Japanese terms or UMLS concept, the final result will be NO if there exists only one NO judgment.

The goal of Phase two was to correct the sets that were judged as NO. On a case by case basis, members discussed the reasons for the mismatch, and members made a final decision by voting via web interface.

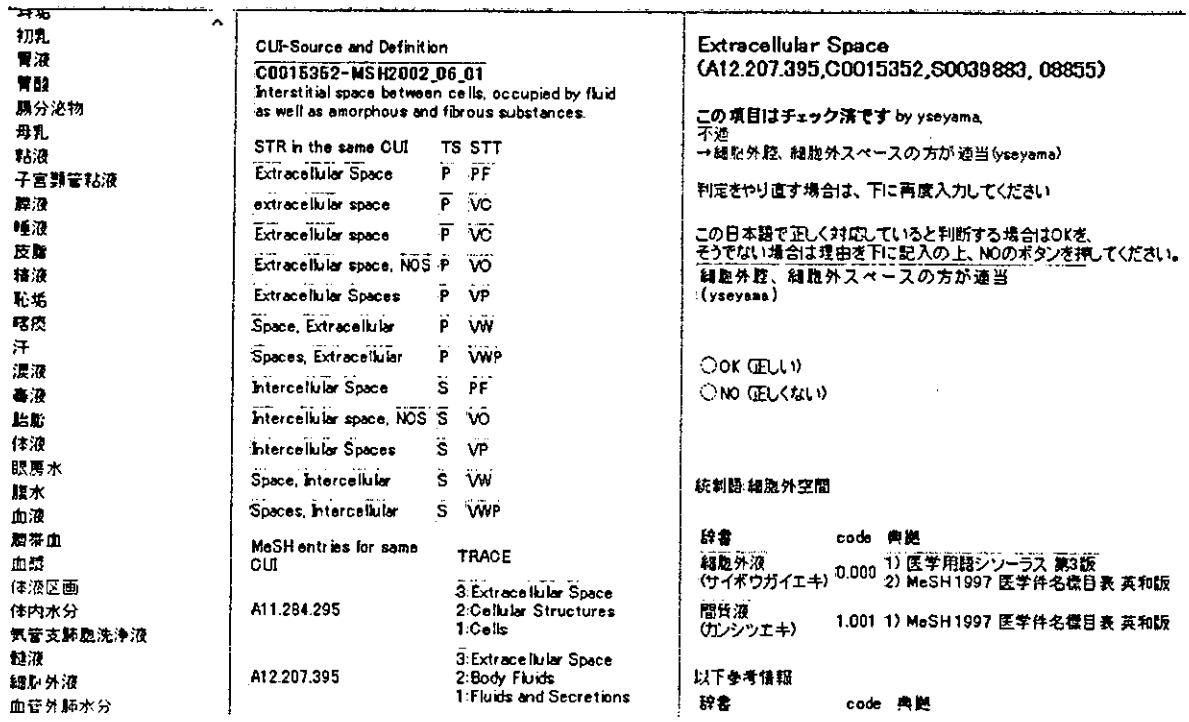

Figure 2 - The left window shows the list of MeSH numbers with their corresponding English primary string and Japanese primary term (here shows only Japanese primary term due to space limitation). When the user selects a MeSH number, the relevant information appears in the middle and right windows. These contents are the same as those in the Figure 1.

Web interface for Phase one judgment

The WWW was used as the medium to verify whether the Japanese terms properly corresponded to the UMLS concepts. Fifteen people with a background in Japanese health related terms participated in this project. Each member individually selected their preferred areas from the top MeSH nodes and checked the validity of the Japanese terms that fell under the chosen nodes.

Figure 1 shows the judging interface. There are two areas in the window. The primary Japanese term and its synonyms are shown on the left side, and corresponding UMLS concept, its definition, and synonyms are shown on the right side. In the upper left region, the top left area is the judging interface. This interface includes a text area for adding comments and OK and NO buttons. Below this, Japanese synonyms and their sources and a table detailing Japanese reference terms that relate to this concept and their sources are displayed. In the right area, the UMLS concept definition, the list of English strings for the concept, and a list of all MeSH numbers for the concept are shown.

Each member judged whether the Japanese terms listed in the synonym table corresponded to the English terms and definitions listed on the right. The member then clicked either the OK or NO button, and the reasons for the decision were detailed in the text box. This process is continued until all of the Japanese terms assigned to a member were completed.

Figure 2 shows an interface in which members can explore all of the MeSH numbers, even those assigned to other members. In this figure, the left window shows only a list of Japanese primary term due to space limitation. But in reality, a list of MeSH numbers and corresponding English primary strings are shown at the left side. When a user clicks on a MeSH number, the information relating to the node appears in the middle and the right windows. The contents of these windows are the same as those in Figure 1.

Web interface for browsing comments given

Figure 3 shows the web interface used to browse the member's comments, which can be examined in real-time. Comments are displayed in the 4th column with the member's name in parentheses. The results of decisions are shown in the 3rd column. Some concepts that were judged as OK were submitted with comments. These concepts will be treated the same as those judged NO in the correction phase.

Web interface for discussions and voting – Phase two judgment

Members are able to submit further opinions for concepts judged as NO or as OK that already contain comments. This additional interface is similar to Figure 1. After a thorough discussion, the changes are proposed. For example, "The word A should be changed to word B in the Japanese synonyms for concept C" will be proposed in Japanese. The final decision is then made by a vote.

Keratinocytes 角化細胞/ケラチン細胞/表皮細胞 A11.436.397	06746 NO	表皮細胞は上位語 (yseyama)	角化細胞/ ケラチノサイト/ ケラチン細胞/ 表皮細胞/ Keratinocyte/ Keratinocytes/ 角質細胞/	
Nucleolus Organizer Region NOR/核小体形成体部/核小体形成域 A11.284.170.279.190.160.650 G05.275.658	06790 NO	AgNORは不適当 (yseyama)	核小体形成域/ AgNOR/ 核小体形成体/ 核仁形成体域/ NOR (Nucleolus Organizer Region)/ Nucleolar Organizer/ Nucleolus Organizer Region/ 核小体形成体部/ AgNORs/ Nucleolar Organizer Regions/ 核小体形成領域/ 仁形成体部/	
Dilatation, Pathologic 病的拡張症/異常拡張症 C23.300.325	06802 NO	拡張症-病理的(hliu)	病的拡張症/ 拡張症-病的/ Dilatation, Pathologic/ Ectasia/ Pathologic Dilatation/ Pathologic Dilation/ 異常拡張症/	

Figure 3 - Members are able to browse comments issued by other members in real time. The first column shows a MeSH descriptor and the corresponding Japanese term, the 3rd column shows current judgment, the 4th column shows the member's comments and the 5th column shows corresponding Japanese terms for the concept.

Results

Phase one judgment was started in January 2003 and was finished in September. Phase two checking is currently in progress. This section presents the results thus far.

Analysis of Phase one judgment

1503 concepts (7.3%) were judged as NO and 1865 (9.1%) were submitted with comments. As previously stated, concepts that included comments were treated the same as those judged as NO., and then we analyzed whole cases being issued any comments. The comments were categorized into the following six groups:

4. A concept contains English terms, and sometimes no Japanese term. (44.0%)
5. There is no Japanese class or group name that corresponds to the plural English form. (11.8%)
6. Other Japanese terms are more suitable and should be included. (33.6%)
7. Some Japanese terms are not appropriate and should be excluded. (5.5%)
8. Some terms are questionable and need further discussion. (2.1%)
9. No change is needed. (2.8%)

Category 1 means that some English terms appear directly in Japanese articles. Category 2 is a feature of Japanese language that there is no explicit plural form of the Japanese noun. Categories 3 through 5 were the intended target of the Phase two process, which number 770 (41.3%). This process, which involves discussion and voting, will be completed within a month.

Estimation of workload for revision of Japanese thesaurus

Fifteen members of professionals relating to Japanese biomedical vocabulary participated in the Phase one work, requiring a total of 124 days. Each member worked approximately a week on the project. The members averaged 167 concepts a day, while one member was able to check a maximum 1920 concepts in only one day.

847 descriptors were added and 47 descriptors were deleted between the 2001 and 2002 MeSH versions, resulting in a total of 894 concepts that needed to be updated in the Japanese thesaurus. From 2002 to 2003, 1250 concepts were added and 20 concepts were deleted, necessitating 1270 new updates.

From these previous experiences, it is estimated that six mandays are required to check 1000 concepts during the Phase one process.

Discussions

Information retrieval via Japanese medical terms

When the Phase two process are completed, professionals will be able to use a Japanese medical thesaurus that corresponds to the UMLS Metathesaurus. This means that Japanese keywords can be used to search for articles in MEDLINE. This will be useful not only for health professionals, but also the Japanese population at large.

However, current UMLS Metathesaurus consists of seven bit ASCII characters. It should be noted that UMLS should have any multi byte character sets, such as UNICODE.

Comparison by concept

In this project, Japanese terms and corresponding English terms were compared for a concept in the UMLS. However, when the UMLS is revised, some of the English terms in a concept will be changed and others will not. When this occurs, a considerable amount of work must be performed on the corresponding set of Japanese terms, because all of the Japanese terms within the concept will need to be checked. Therefore, just as the UMLS introduced the CUI-LUI-SUI scheme, the Japanese terms must be managed efficiently while updating the identification system. An option is to introduce an LUI for Japanese terms that correspond to the English strings that have the same LUI and the same

mental meaning in UMLS. Table 1 shows one such example. This table displays the relationship between the English and Japanese terms for the concept "Eye". A kanji character in upper two rows and the former character in lower three means "eye". The latter kanji character in lower three rows means "ball". As is evident from this example, introducing an LUI on Japanese side may dramatically reduce the workload during the UMLS concept updates.

Table 1: Sample relationships between English and Japanese

UMLS LUI	English	Japanese
L0015392	Eye, eyes	眼
L0876007	Oculus	眼
L0015418	Eyeball	眼球
L1811070	Bulbus oculi	眼球
L0847402	Globe	眼球

A working style for collaborating on the Web

This project required the development of web interfaces to view the relationships between English and Japanese terms within a UMLS concept, make judgments and submit comments, discuss the issues, and vote on a decision. These interfaces were extremely useful and efficient for the participating members.

Some members, however, reported that it was difficult to understand the judgment policy and the remarks form when they first started. During this study, the judgment policy was added to the web site. Periodic meetings were necessary even though the judgment process was conducted remotely over the Web.

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References

[1] Lindberg D, Humphreys B, McCray A. The Unified Medical Language System. *Methods Inf Med* 1993; 32(4): 281-91.

[2] Campbell KE, Oliver DE, et al. Representing Thoughts, Words, and Things in the UMLS. *JAMIA*. 1998;5:421-31.

[3] Cimino JJ. Auditing the Unified Medical Language System with Semantic Methods. JAMIA. 1998:5;42-51.

[4] Bodenreider O, McCray AT. From French vocabulary to the Unified Medical Language System. *Medinfo*. 1998; 9 Pt 1:670-4.

[5] Hersh WR, Donohoe LC. SAPHIRE International: a tool for cross-language information retrieval. *Proceedings/AMIA Annual Symposium*. 1998; 673-7.

[6] Tanaka M. A Mapping Approach of Japanese Medical Vocabulary to UMLS. *Proceedings/Japan Congress of Medical Informatics* 2000; 920-1

[7] Liu Y, Satomura Y. Building a Controlled Health Vocabulary in Japanese. *Method Inform Med* 2001; 40(4): 307-14.

[8] Hatano K, Hamada A, et.al. Developing of Clinical Disease Name Classification Based on ICD 10-based Code Set of Disease Names. *Proceedings/Japan Congress of Medical Informatics* 2001; 739-41

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CpG Island Methylator Phenotype Is a Strong Determinant of Poor Prognosis in Neuroblastomas

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Abstract

Neuroblastoma, one of the most common pediatric solid tumors, is characterized by two extreme disease courses, spontaneous regression and life-threatening progression. Here, we conducted a genome-wide search for differences in DNA methylation that distinguish between neuroblastomas of the two types. Three CpG islands (CGI) and two groups of CGIs were found to be methylated specifically in neuroblastomas with a poor prognosis. By quantitative analysis of 140 independent cases, methylation of all the five CGI (groups) was shown to be closely associated with each other, conforming to the CpG island methylator phenotype (CIMP) concept. The presence of CIMP was sensitively detected by methylation of the *PCDHB* CGIs and associated with significantly poor survival (hazard ratio, 22.1; 95% confidence interval, 5.3-93.4; $P < 0.0001$). Almost all cases with N-*myc* amplification (37 of 38 cases) exhibited CIMP. Even in 102 cases without N-*myc* amplification, the presence of CIMP (30 cases) strongly predicted poor survival (hazard ratio, 12.4; 95% confidence interval, 2.6-58.9; $P = 0.002$). Methylation of *PCDHB* CGIs, located in their gene bodies, did not suppress gene expression or induce histone modifications. However, CIMP was significantly associated with methylation of promoter CGIs of the *RASSF1A* and *BLU* tumor suppressor genes. The results showed that neuroblastomas with CIMP have a poor prognosis and suggested induction of silencing of important genes as an underlying mechanism. (Cancer Res 2005; 65(3): 828-34)

Introduction

Epigenetic abnormalities, especially alterations in DNA methylation, are intimately involved in development of various human tumors (1). Aberrant methylation of promoter CpG islands (CGI) causes inactivation of tumor suppressor genes. Genomic instability is caused by genomic hypomethylation and is associated with hypermethylation (2, 3). Identification of epigenetic abnormalities in human cancers is expected to lead not only to discovery of novel disease mechanisms but also to development of new diagnostic markers. Therefore, we previously developed a genome-wide scanning method, methylation-sensitive representational difference analysis (MS-RDA), for detecting differences in DNA methylation (4, 5). This technique analyzes unmethylated, CpG-rich regions of the genome and has already identified genes silenced in human lung, stomach, breast, and pancreatic cancers (6-9).

Neuroblastoma derived from primitive cells of the sympathetic nervous system is one of the most common solid tumors in childhood, characterized by two extreme disease courses, spontaneous regression, and life-threatening progression (10, 11). The clinical outcome is associated with disease stage, age at diagnosis, histologic classification, N-*myc* amplification, DNA ploidy, and *TrkA* overexpression (10-12). These characteristics are therefore used to classify cases into low-, intermediate-, and high-risk groups. However, especially in the cases with intermediate risk, prediction of prognosis and therapeutic decision-making are still difficult, and development of new markers is an urgent priority. Moreover, the molecular bases underlying the two distinct clinical courses are still unknown, and their clarification is needed to allow development of novel therapeutics.

In the present study, considering the major involvement of epigenetic machinery in embryonic development (13, 14), we searched for differences in DNA methylation between neuroblastomas with a good prognosis and counterparts with a poor prognosis by MS-RDA.

Materials and Methods

Tissue Samples and Cell Lines. Tumor samples were obtained from 145 nonrecurrent cases between 1995 and 1999 and were used under approval of institutional review boards. The mean age at initial diagnosis was 27 months (range, 0-216 months). Their clinical stages were determined according to the International Neuroblastoma Staging System, and 40, 17, 20, 60, and 8 cases belonged to stages I, II, III, IV, and IVS, respectively. Normal adrenal medulla tissue was collected from a case undergoing nephrectomy for a renal cancer. Neuroblastoma cell lines were obtained from the American Type Culture Collection (Manassas, VA), the Japanese Collection of Research Bioresources (Tokyo, Japan), and the RIKEN Bio Resource Center (Tsukuba, Japan). GANB was established by A.N. and normal human bronchial epithelial cells were purchased from Cambrex (East Rutherford, NJ). High molecular weight DNA and total RNA were extracted as previously described (7). Total RNAs of brain and adrenal glands were purchased from Clontech (Palo Alto, CA).

MS-RDA and Database Search. MS-RDA was done as previously described (4, 5). Genomic DNA of primary neuroblastomas with a good prognosis (cases 92, 98, 104, 112, and 148) and neuroblastoma cell lines established from cases with a poor prognosis (CHP134, IMR32, GANB, NGP, and TGW) were digested with *Hpa*II, and then two pooled DNA samples were prepared. Although use of cell lines is highly recommended for MS-RDA (5), no cell lines were available for neuroblastomas with a good prognosis, and therefore we used the primary samples. To isolate CGIs that were hypermethylated in the latter, the cell line pool was used as the tester, and the primary tumor pool as the driver. MS-RDA in the opposite direction

Note: Supplementary data for this article are available at Cancer Research online (http://cancerres.aacrjournals.org/).

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