



手島昭樹

(無題)

2 件のメッセージ

三木恒治

宛先:

2008/11/06 18:46

手島先生

班会議の資料ですが今回は特にないのが現状です。泌尿器科学会のがん登録もようやく今年再開し、泌尿器科学会専門医教育施設 1184 施設に依頼し、今年中に膀胱がんの登録をまずやることになりました。
会員の負担を考え前立腺がんは来年ということにいたしました。今後のがん登録の予定ですが

2008年 2002 年に診断された膀胱癌症例

2009年 2004 年に診断された前立腺癌症例

2010年 腎孟尿管癌と精巣腫瘍

という順でやる予定です。

京都府立医科大学大学院医学研究科

泌尿器外科学・腫瘍薬剤制御学講座

三木 恒治

〒602-8566

京都市上京区河原町広小路梶井町465番地

Tel :

Fax :

E-Mail :

手島昭樹

宛先: 三木恒治

Cc: Hodaka Numasaki

2008/11/06 20:05

三木先生

JPCS03-05を含むquality indicator

前立腺癌

福岡大学
中村和正

Patient eligibility criteria in the Japanese PCS for prostate cancer

- Adenocarcinoma of the prostate
 - No distant metastases
 - No prior or concurrent malignancies
 - No previous radiation therapy
- * Patients who received radical prostatectomy or hormonal therapy prior to radiotherapy were included.

Category and number of the patients surveyed

Category	1996-1998	1999-2001	2003-2005
Fresh (Radical radiotherapy with photon)	161(51.8%)	283(53.6%)	354(70.0%)
Surgery (Radiotherapy after prostatectomy)	64(20.6%)	105(19.0%)	94(18.6%)
H-ref. (Radiotherapy for hormone-refractory ca.)	58(18.8%)	96(18.2%)	34(6.7%)
Others	28(9.0%)	44(8.3%)	24(4.7%)
Total number	311(100%)	528(100%)	506(100%)
* brachytherapy(HDR or LDR)14(4.5%)	38(7.2%)	23(4.6%)	

> There has been a decline in the fraction of patients treated for H-ref. cancer.

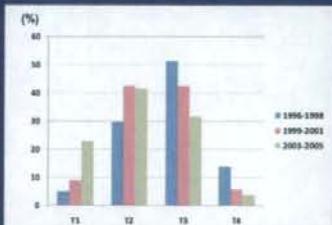
Age (median)

Category	1996-1998	1999-2001	2003-2005
Fresh (Radical radiotherapy with photon)	46-89 y (70)	49-92 y (71)	50-87 y (71)
Surgery (Radiotherapy after prostatectomy)	49-83 y (69)	36-89 y (67)	53-81 y (69)
H-ref. (Radiotherapy for hormone-refractory ca.)	55-86 y (73)	51-94 y (73)	47-90 y (76)

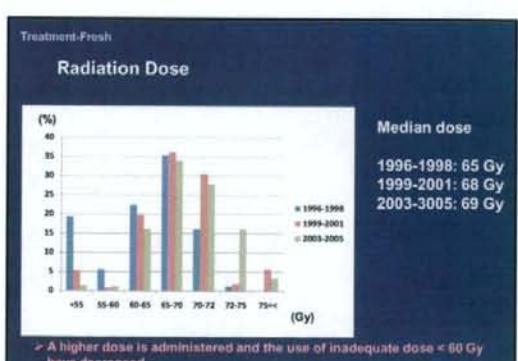
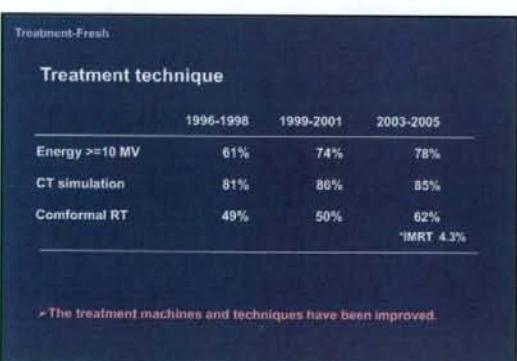
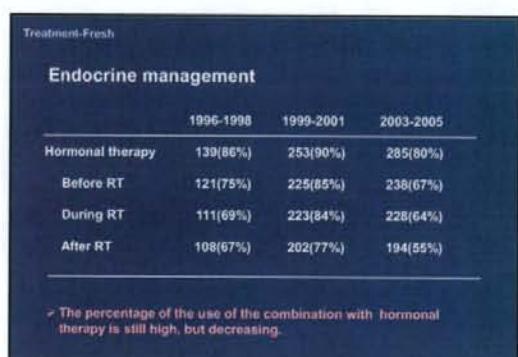
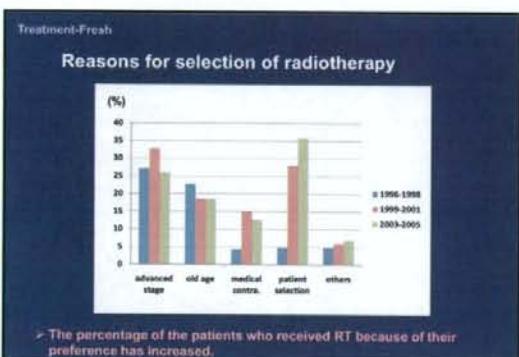
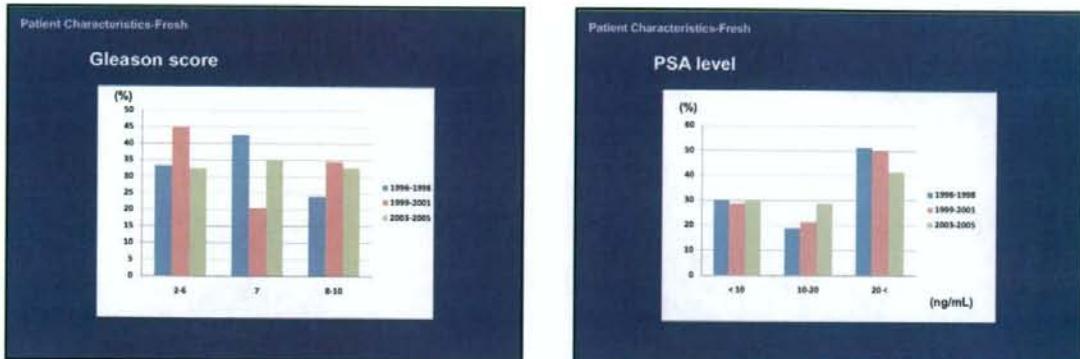
Changing trends in the practice for radical radiotherapy for clinically localized prostate cancer

Patient Characteristics-Fresh

T-stage



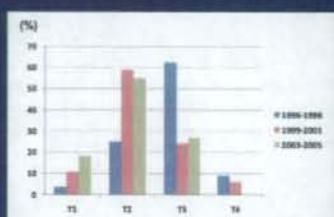
> There has been a decline in the fraction of patients with T3 or T4 tumors.



Changing trends in the practice for radiotherapy after prostatectomy

Patient Characteristics-Surgery

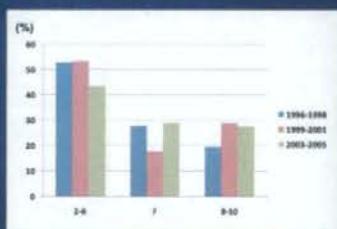
T-stage before surgery



→ There is a decline in the fraction of patients with clinical T3-4 tumors before surgery.

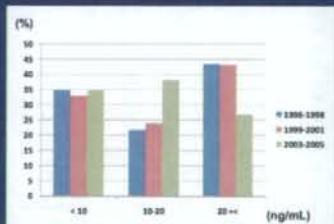
Patient Characteristics-Surgery

Gleason score



Patient Characteristics-Surgery

PSA level before surgery



Treatment-Surgery

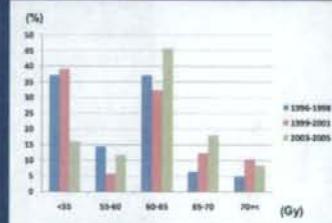
Endocrine management

	1996-1998	1999-2001	2003-2005
Hormonal therapy	84%	73%	49%
Before RT	83%	74%	46%
During RT	59%	53%	25%
After RT	59%	57%	21%

→ The percentage of the patients treated in combination with hormonal therapy has decreased.

Treatment-Surgery

Radiation Dose



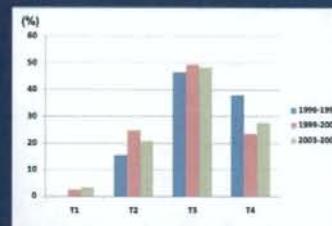
Median dose

1996-1998: 60 Gy
1999-2001: 60 Gy
2003-2005: 60 Gy

Changing trends in the practice for radiotherapy for localized hormone refractory prostate cancer

Patient Characteristics-H-ref

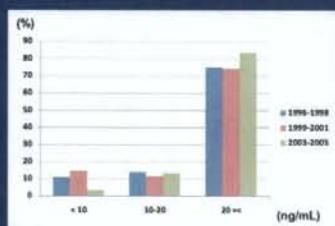
T-stage



➤ The distribution of T-stages and Gleason scores (data not shown) has not been changed.

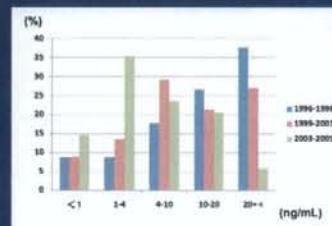
Patient Characteristics-H-ref

PSA level before androgen ablation



Patient Characteristics-H-ref

PSA level before radiotherapy



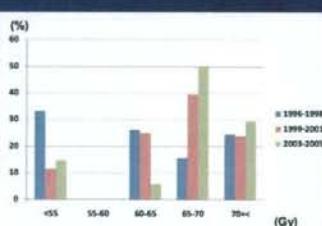
➤ Radiotherapy has been performed with a lower level of PSA after progression from hormonal therapy.

Treatment-H-ref

Radiation Dose

Median dose

1996-1998: 60 Gy
1999-2001: 60 Gy
2003-2005: 68 Gy



➤ A Higher doses has been irradiated.

まとめ－1

根治照射例

T3-4症例が減少

患者自ら放射線治療を希望する症例が増加
ホルモン療法併用割合がわずかだが減少
放射線治療装置、技術は向上
投与線量は増加

まとめー2

術後照射例

T3-4症例が減少
ホルモン療法併用例は減少
投与線量は不变

ホルモン不応・抵抗例

症例数が全体に占める相対的割合は低下している
PSAが低いレベルで照射が開始される症例が増加
投与線量は増加

PCSを含むJNCDBは、前立腺癌の放射線治療の内容、質の変化を明らかとするQuality indicatorとなり得る

External Beam Radiotherapy for Clinically Localized Prostate Cancer: Clinical Significance of Nadir Prostate-Specific Antigen within 12 Months

Kazuhiro Ogawa, Katsumasa Nakamura, Tomoharu Sasaki, Hiroshi Onishi, Masahiko Koizumi, Yoshiyuki Shiota, Masayuki Araya, Nobutaka Mukumoto, Michihide Mitsumori and Teruki Teshima

Department of Radiology, University of the Ryukyus, Okinawa, Japan
and Japanese Patterns of Care Study Working Subgroup of Prostate cancer

Purpose

To analyze retrospectively the results of external beam radiotherapy for clinically localized hormone-refractory prostate cancer (HRPC).

To investigate the clinical significance of nadir prostate-specific antigen (PSA) within 12 months (nPSA12) as an early estimate of clinical outcomes after radiotherapy.

nPSA12 (nadir prostate-specific antigen within 12 months)

- Defined as the lowest PSA level achieved during the first year after completion of radiotherapy
- Median number of PSA evaluation within 12 months was 4 times (range: 1-12)
- All patients without clinical failure had at least 1-year follow-up.

Methods and Materials

Patient population

Data from Japanese Patterns of Care Study (PCS) Survey
(Survey between 1996-2001)

Total number of pts surveyed.	839
Clinically localized HRPC	154
Pts. with sufficient nPSA12 data	84

All 84 patients received androgen ablation initially

Methods and Materials

Eighty-four patients with localized HRPC treated with external beam radiotherapy were retrospectively reviewed.

Total radiation dose: 30-76 Gy (median: 66 Gy)

The median follow-up in all 84 patients was 26.9 months (range, 2.7-77.3 months).

Patient and Treatment Characteristics

Median age:	73 years	< 75: 51 pts	≥ 75: 33 pts
KPS:	> 80%: 35 pts	≤ 80%: 45 pts	Unk: 4 pts
T stage	T0-2: 18 pts	T3-4: 56 pts	
N stage	NO: 58 pts	NI: 10 pts	Unk: 16 pts
Gleason Score	< 6: 5 patients	> 6: 13 pts	Unk: 66 pts

Patient and Treatment Characteristics

Pre-treatment PSA (median: 29.8 ng/ml)

< 20 ng/ml:	14 pts
≥ 20 ng/ml:	45 pts
Unk:	25 pts

Pre-radiotherapy PSA (median: 9.7 ng/ml)

< 4 ng/ml:	14 pts
≥ 4 ng/ml:	69 pts
Unk:	1 pts

Patient and Treatment Characteristics

Hormonal therapy (alone or in combination)

Orchiectomy	19 pts (12%)
Estrogen agent	24 pts (28%)
LH-RH agonist	78 pts (92%)
Antiandrogen	60 pts (71%)

Chemotherapy

Yes	23 pts (27%)
No	58 pts (69%)
Unk	3 pts

Patient and Treatment Characteristics

Radiotherapy

Radiation field

WP plus boost	34 pts (40%)
Prostate only	50 pts (60%)

Total radiation dose (Gy)

< 60	12 pts (14%)
≥ 60	72 pts (86%)

CT-based treatment planning

Yes	17 pts (20%)
No	49 pts (59%)

Conformal therapy

Yes	23 pts (27%)
No	44 pts (53%)

Statistical Analysis

For the assessment of differences between groups

The chi-square test
The Student's t test
Log-rank test

For the assessment of treatment outcome

Kaplan-Meier method
Cox regression model

A probability level of 0.05 was chosen for statistical significance.

Statistical analysis: SAS analysis system

Results

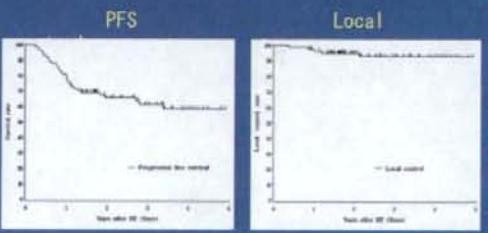
- Survival (3-year)

OS	67%
PFS	61%
Local control	93%

- Site of recurrence

DM and/or regional (40%)	34 patients
Local progression (6%)	5 patients

PFS and Local Control



Results

Median nPSA12:

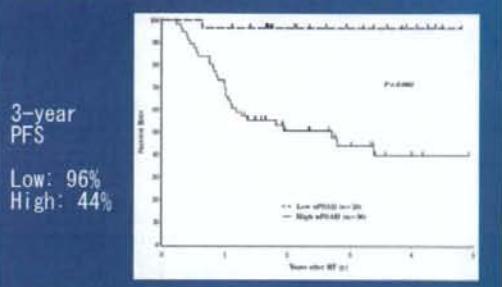
Clinical failure	3.1 ng/ml
Without clinical failure	0.5 ng/ml

3-year PFS rates:

low nPSA12 (< 0.5 ng/ml)	96%
High nPSA12 (≥ 0.5 ng/ml)	44%

($p < 0.0001$)

PFS according to the level of nPSA12



Results

Prognostic factors concerning PFS

Univariate analysis

	P value
nPSA12	0.0029
Pre-treatment PSA	0.0260

Multivariate analysis

	RR (95%CI)	P value
nPSA	10.965 (1.45-82.671)	0.020

Late toxicity

	Grade 3	Grade 4	Total dose
Rectal			
Bleeding	5	0	61-71 Gy
Stricture	1	0	66 Gy
Urinary			
Incontinence	0	0	-
Stricture	1	0	50 Gy
CT-based treatment planning:	1 / 7 patient	(14%)	
Conformal therapy:	2 / 7 patients	(29%)	

Conclusions

- External beam radiotherapy had an excellent local control rate for clinically localized hormone-refractory prostate cancer.
- nPSA12 was predictive of clinical outcomes after radiotherapy.

前立腺癌グループ

術後照射における最近の知見
と
CaPSURE

日本PCS前立腺癌小作業部会
荒屋正幸 大西洋 中村和正 小泉雅彦
小川和彦 光森通英 手島昭樹

術後照射

最近の知見

- Adjuvant療法
 - 3つの randomised trial
 - EORTC 22911
 - SWOG 8794
 - ARO 96-02 / AUO AP 09/95

- EORTC 22911

pT2-3, pN0M0, R1 or ECE or SVI ,
1005 pts,
ART=60Gy(502 pts) v.s. "wait and see"(503 pts)

EORTC: The European Organization for Research and Treatment of Cancer

- SWOG 8794

pN0/cN0, ECE and/or SVI or R1
425 pts,
ART=60~64Gy (214 pts) v.s. Observation (211pts)

SWOG: Southwest Oncology Group

- ARO 96-02 / AUO AP 09/95

pT3pN0M0
307 pts
ART=60Gy (114 pts) v.s. Observation (159 pts)

German Intergroup trial ARO 96-02/AUO AP 09/95

Biochemical progression-free survival

		RP	RP+ART
EORTC	5year	52.6%	74.0%
SWOG	5year	~44%	~73%
	10year	~28%	~52%
ARO / AUO AP	5year	54%	72%

Adjuvant Radiotherapy for Patients with Locally Advanced Prostate Cancer - A New Standard? Ute Ganewindt, et al. European Urology 54 (2008) 528-542

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Adjuvant Radiotherapy

- 経過観察群よりも、生化学的無増悪率(5年/10年)は良好
- 粗生存率に関しては、統計学的有意差なし

Adjuvant RT v.s. Salvage RT

Adjuvant RT v.s. Salvage RT

There was a significant reduction in biochemical failure with ART compared with SRT.

- The 5-year freedom from biochemical failure (FFBF) from surgery was 75% after ART, compared with 66% for SRT (hazard ratio [HR]=1.6, $P=.049$).
- The 5-year FFBF from the end of RT was 73% after ART, compared with 50% after SRT (HR=2.3, log ratio [LR] $P=.0007$).
- From the end of RT, SRT and Gleason score ≥ 8 were independent predictors of diminished FFBF. From the date of surgery, Gleason score ≥ 8 was a significant predictor of FFBF.

A Multi-Institutional Matched-Control Analysis of Adjuvant and Salvage Postoperative Radiation Therapy for pT3-4N0 Prostate Cancer.
Eduardo J. Trabulsi, et al. Urology. 2008 Jul 29.

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術後照射を行う理由の変化

	'99-01		'03-05	
	A	B	A1	B1
・ 断端陽性			8	6
・ 断端陰性だが局所進行または高リスク	33	28	(1) 2 (?) 1	
・ 微域リンパ陽性			2	0
・ PSA正常化せず	2	0	1	0
・ PSAの再上昇	3	2	(1) 4	
・ その他	1	0	1	0
・ 不明/欠損	(13)	(8)	(0)	(0)

術後照射を行う理由の変化

	'99-01		'03-05	
	A	B	A1	B1
・ Adjuvant RT	43	38	(1) 2 (?) 1	
・ Salvage RT	2	0	1	0
・ その他	9	2	(1) 4	
・ 不明/欠損	(13)	(8)	(0)	(0)

その他の話題提供

- Predicting PSA failure following salvage radiotherapy for a rising PSA post-prostatectomy: from the CaPSURE database.
Macdonald OK, et al. Urol Oncol. 2008 May-Jun;26(3):271-5.
- Adjuvant radiotherapy in prostate cancer: predictors of prostate-specific antigen recurrence from the CaPSURE database.
Macdonald OK, et al. Urology. 2007 Jul;70(1):106-10.
- Quality of Life in Men With Locally Advanced Adenocarcinoma of the Prostate: An Exploratory Analysis Using Data From the CaPSURE Database.
White WN, et al. J Urol. 2008 Dec;180(6):2409-14.

CaPSURE database ?

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CaPSURE

Cancer of the Prostate Strategic Urologic Research Endeavor

CaPSURE

Cancer of the Prostate Strategic Urologic Research Endeavor

- To document the impact of prostate cancer on
 - Resource utilization
 - Clinical outcomes
 - Health-related quality life
 - Survival in typical practice setting

The CaPSURE database: a methodology for clinical practice and research in prostate cancer.
Debrad P, Lubeck, Mark S, et al. Urology. 1996 Nov; 48(5):773-7.



- Randomized clinical trial
実臨床的ではない、
結果を出すのに費用、時間がかかる
- Observational databases
限られた地域でのRCTと、とてもなく数多くの状況が反映した文献とのギャップを埋めることができる
リアルタイムな情報を得ることができる
RCTに対して相補的な存在、競合するものではない

PCS/JNCDB と CaPSURE 類似点

- To document the impact of prostate cancer on
 - Resource utilization
 - Clinical outcomes
 - Health-related quality of life
 - Survival in typical practice setting

Data collected from two sources.

- The physician: **Urologist**, at each office visit.
 - Enrolls eligible patients into the study
 - Completes a medical history
 - Records current status, treatment and laboratory results.

PCS/JNCDB と CaPSURE 相違点

- To document the impact of prostate cancer on
 - Resource utilization
 - Clinical outcomes
 - Health-related quality of life
 - Survival in typical practice setting

Data collected from two sources.

• The patient:

- Completes quarterly questionnaires on
 - ①health-related quality of life
 - ②resource utilization
 - ③work loss
 - ④satisfaction with care

- 患者自身にもアンケート方式にて、生活の質・治療に対する満足度のようなものを調査している。

- PCS/JNCDBでは、患者側因子としては医療者側の視点での有害事象としてしか調査されていない。

The World Health Organization defines health as "not merely the absence of disease, but complete physical, psychological and social well-being."

結局、治療の良し悪しは 患者満足度で決まる！

The World Health Organization defines health as

"not merely the absence of disease, but complete physical, psychological and social well-being."

JNCDBが最終的に患者に還元されることを目標にするならば、将来的には、「患者自身の治療に対する満足度」のような患者主体の項目をつくる必要が出てくるのでは。
JNCDBでも追加を検討？

Rather than being based only on clinical presentation and disease progression, decisions about treatment receipt for some men are influenced by cancer related anxiety.

Men should be provided with more psychosocial support to perhaps delay treatment and the ensuing decrements in health related quality of life.

The relationship between anxiety and time to treatment for patients with prostate cancer on surveillance. Latini DM, et al. J Urol. 2007 Sep;178(3 Pt 1):826-31; discussion 831-2.

平成20年度第1回学術年会
'08.11.15(Sat.)
於 国立がんセンター中央病院腎臓腫瘍科会議室

前立腺癌小線源治療の動向とDB



JNCDB前立腺癌RTグループ
○小泉 雅彦
中村 和正、小川 和彦、大西 洋

最近10年間の前立腺癌小線源治療

- 前立腺癌への小線源治療は、この10年間で最も治療体系が塗り変り、適応拡大した分野
- PSA導入で早期症例の急激な増加
- ホルモン治療の進歩で局所治療の重要性増加→手術 or 外照射 or 小線源の多様な局所治療手段の適応拡大と方法の進歩
- 日本では從来、少數施設でHDRが施行
- '03年I-125シードの保険適応が最大のインパクト
→早期例に爆発的な適用拡大

前立腺癌小線源治療の大幅拡大

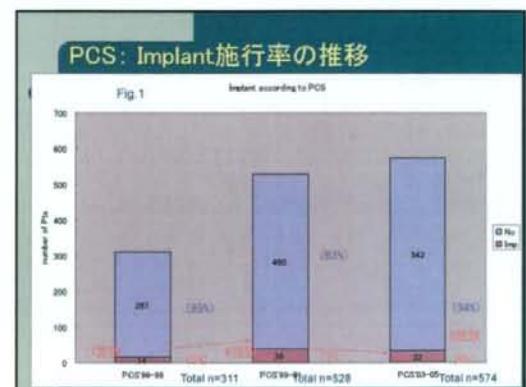
- 日医放専門医会ガイドライン'04で外照射中心の記述中の僅か6行→'08では一章立8頁の大幅増
- JASTRO'00口演1題→'08口演18題、展示23題
- JRS'97/98皆無→'08口演6題、展示8題
- やはりI-125シード療法の適応拡大の寄与が大きい
- シードの全国前向きコホート登録J-POPSも'05～'07.10で2700件となり、「10末まで延長され8000件の登録が期待されている。'08.5 ASCO annual meetingにて発表された

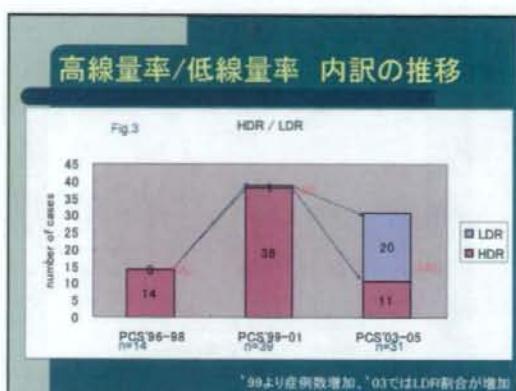
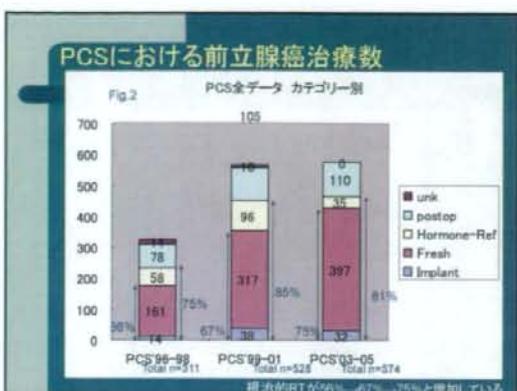
今回のPCS解析の目的

前立腺癌小線源治療の、この10年間のPCS-DB '96-98、'99-01、'03-05を比較検討する

- 適用率と内容の推移
- Quality indicatorとしての
 - 方法(TRUS, template, 刺入経路など)
 - 線量
- についての実態を報告し、その動向を論じる
- 今後のDBのあり方について述べる

治療数・適用内容



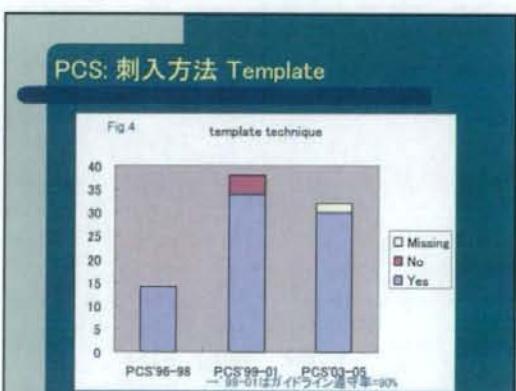


組織内照射適応患者

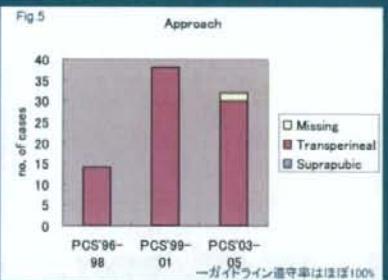
	PCS' 96-98	PCS' 99-01	PCS' 03-05
症例数:	14例 (4.5%)	38例 (7.4%)	32例 (5.6%)
施設数:	1	4	8(全体の14%)
年齢:	71.7 (63.4-82.8)	79.0 (45.5-81.3) [†]	67.3 (52.4-82.4) [†]
NM:	全例cNOMO	全例cNOMO	31例cNOMO
カテゴリー: 不詳	新鮮34例(90%)	新鮮32例(100%)	
	ホルモン不応4例(10%)		
線量率:	全例HDR (線源) Ir-192	HDR37例 (Ir-192)	HDR11例(35%) (Ir-192)
		LDR1例のみ (Au-198)	LDR20例(65%) (I-125, 2例Ir-192)

[†]med (min-max)

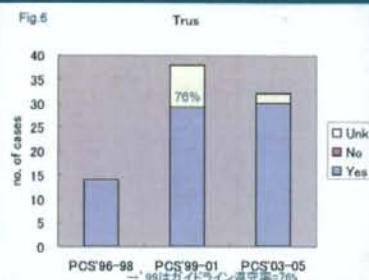
方 法



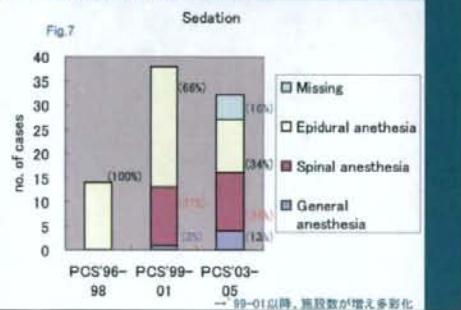
PCS: 刺入方法 Approach



PCS: 刺入方法 TRUS



PCS: 刺入方法 Sedation



線量分割

PCS: Dose & Fractionation

PCS' 96-98

PCS' 99-01

- HDR: ほぼ16.5Gy/3fr/2d* 15-37.5Gy/3-5fr/2-4d*
1例のみ36Gy/6fr/11d

*p=0.025

- 外照射: 全例併用† 全例併用†

ほぼ60Gy/30fr/6w‡ 50-65Gy/15-25fr/15-45d‡

‡p<0.0005

†—ガイドライン遵守率100%

PCS: Dose & Fractionation

PCS' 03-05

HDR: 15-18Gy/2fr/1d: 6例 37.5Gy/5fr/3d: 4例

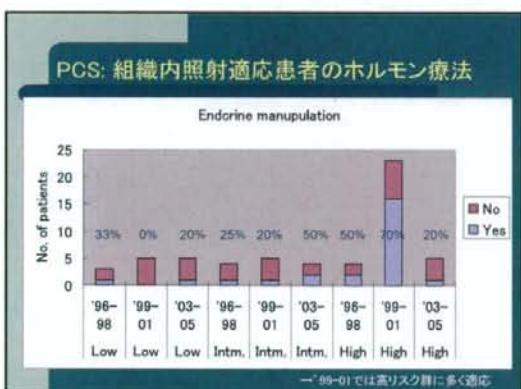
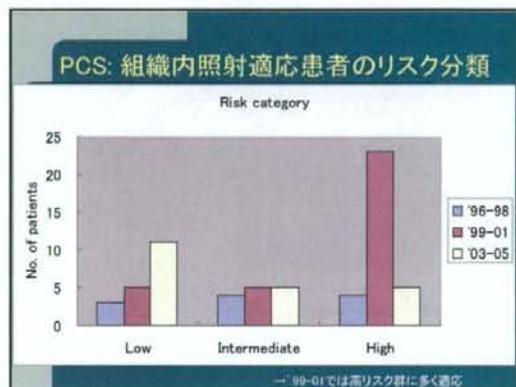
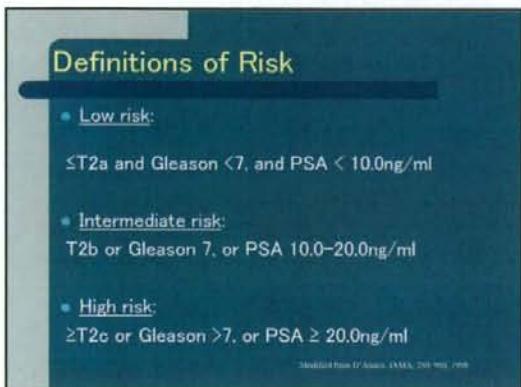
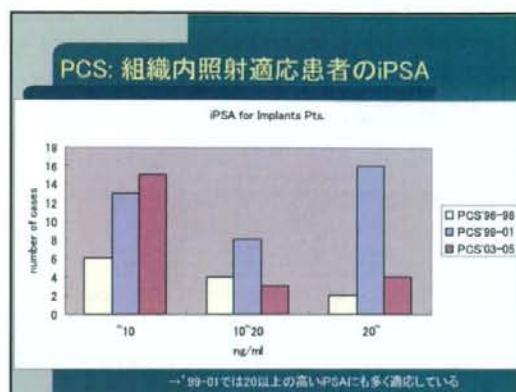
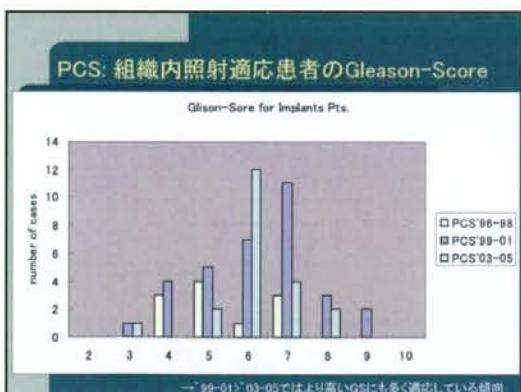
外照射併用

- 1例のみ54Gy/9fr/5dで小線源単独

LDR: 組織内単独 144Gy:6例† 145Gy:12例†

辺縁配置20% 辺縁配置変法76% 均一配置法4%

†—ガイドライン遵守率100%



參考資料