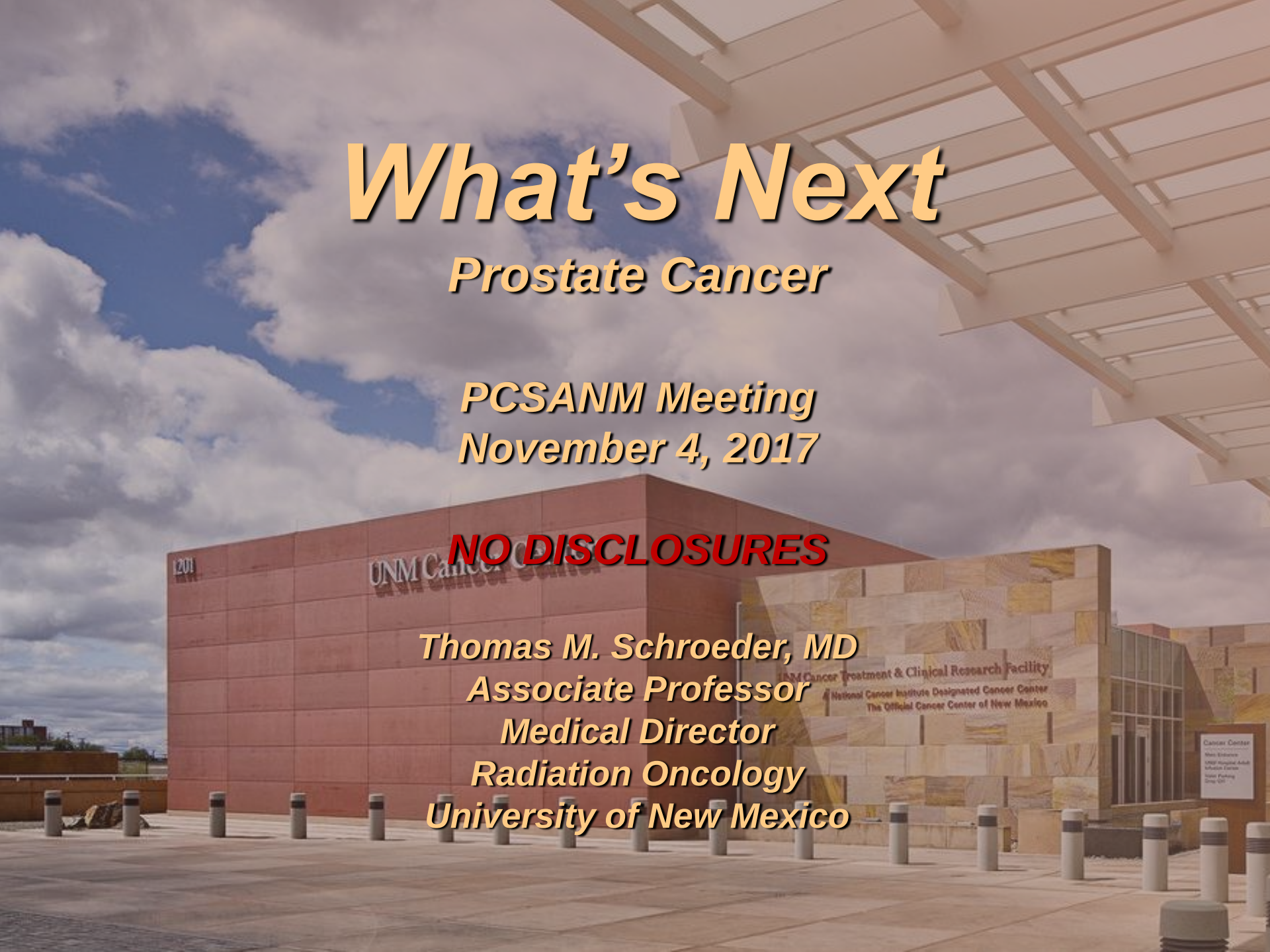


What's Next

Prostate Cancer

PCSANM Meeting
November 4, 2017

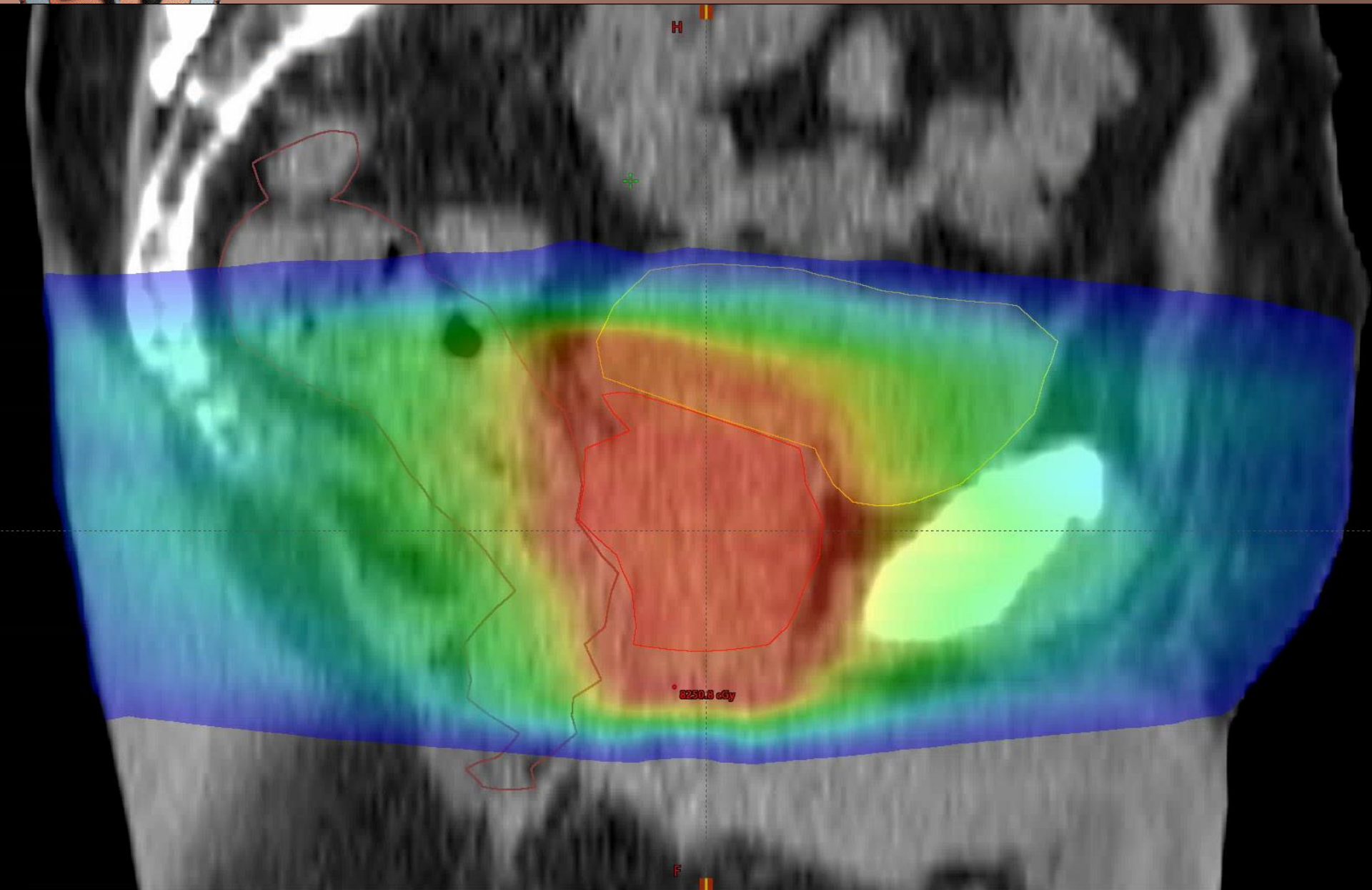
NO DISCLOSURES

Thomas M. Schroeder, MD
Associate Professor
Medical Director
Radiation Oncology
University of New Mexico

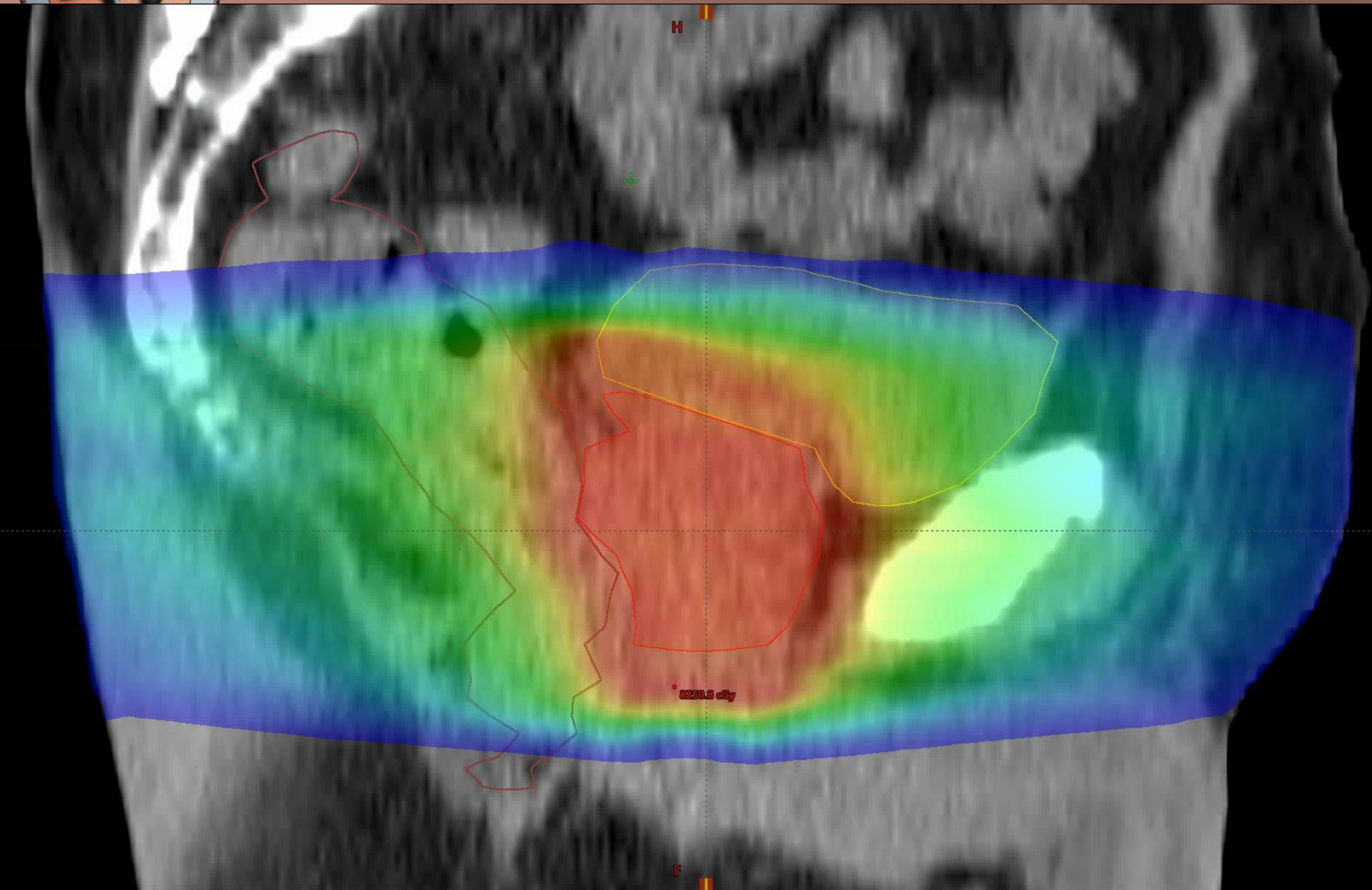
OUTLINE

- SpaceOAR®
- Axumin™
- Oligometastasis
- Wild Speculation
- Questions

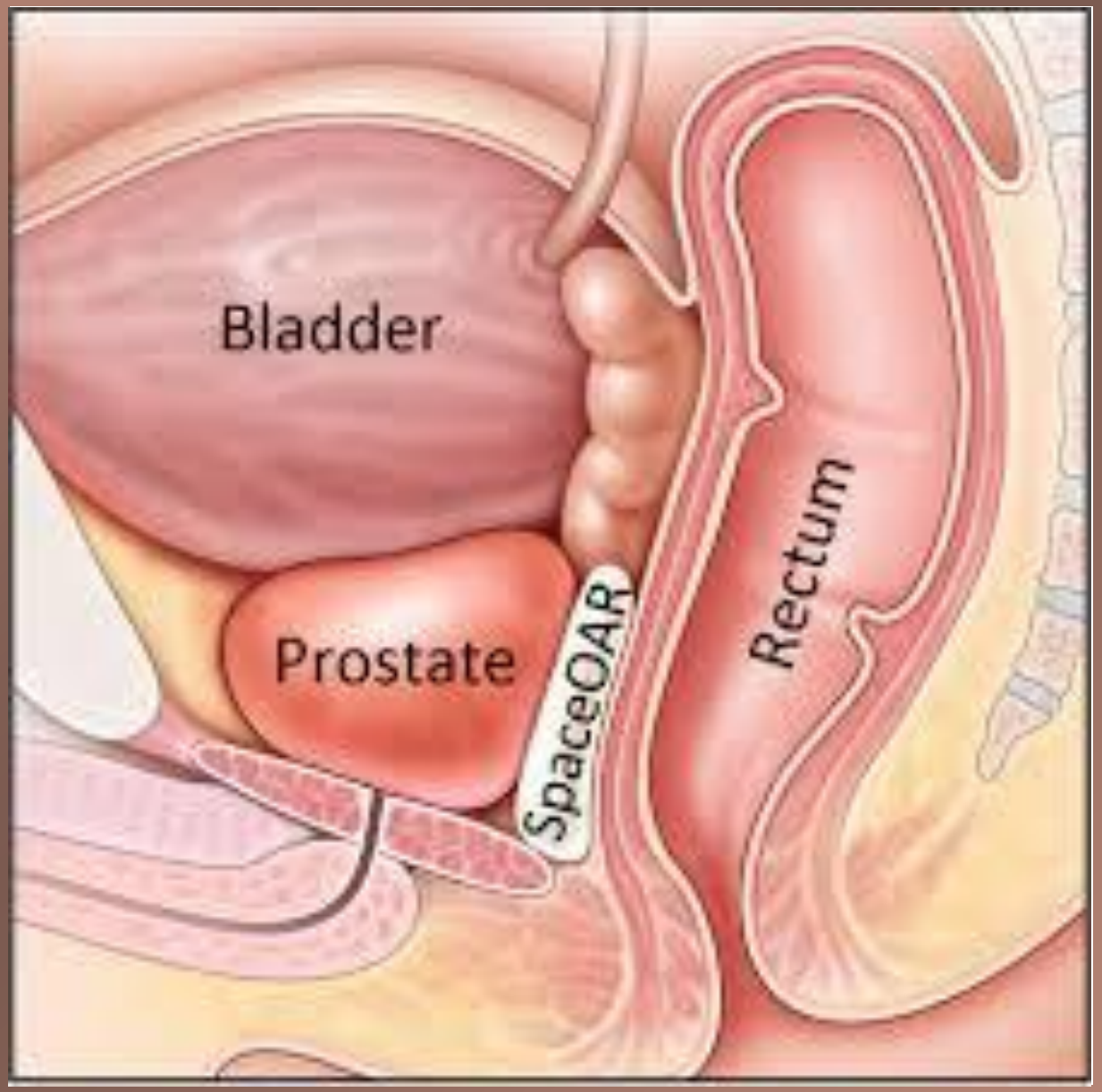
SpaceOAR®



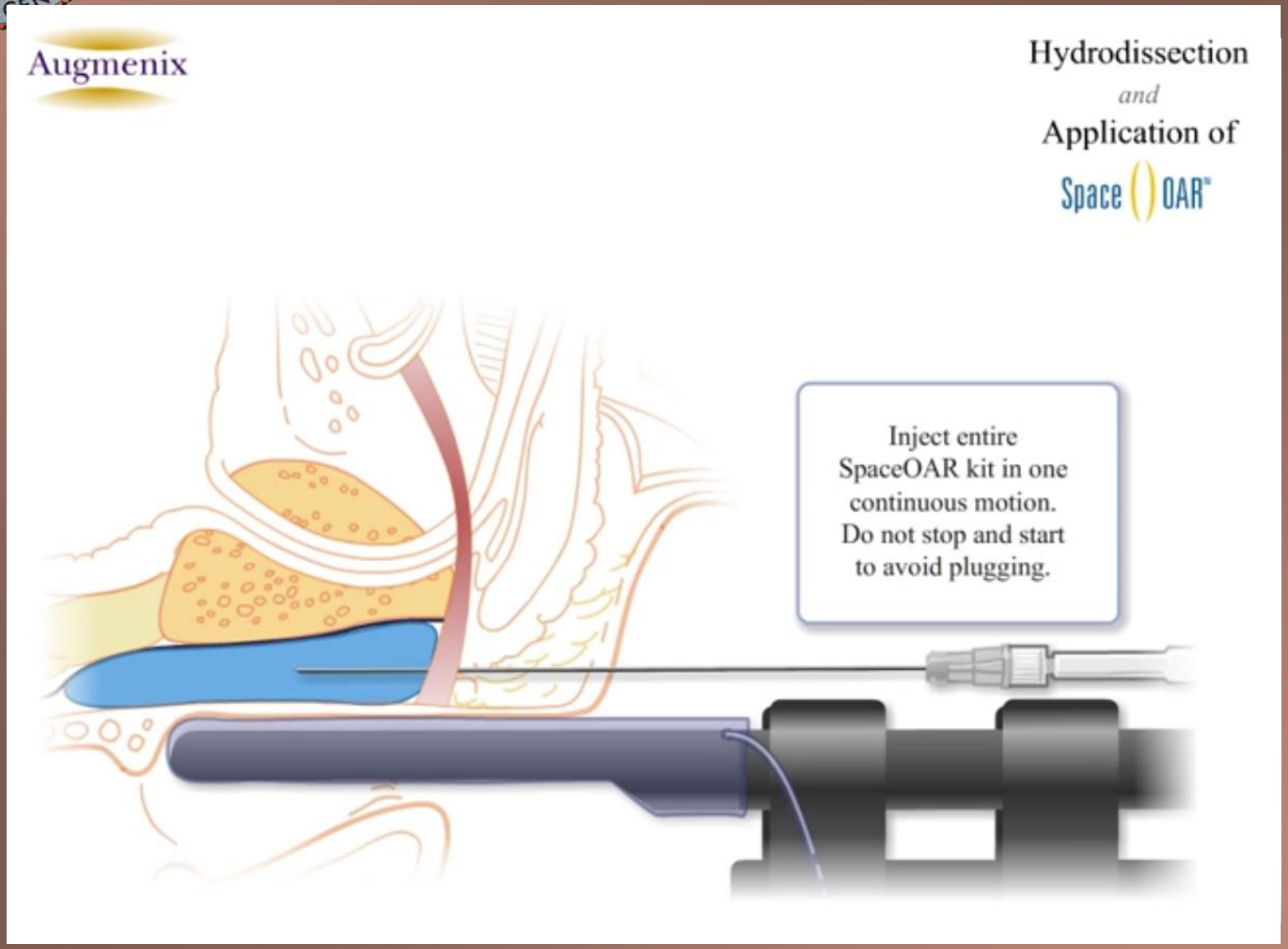
SpaceOAR®



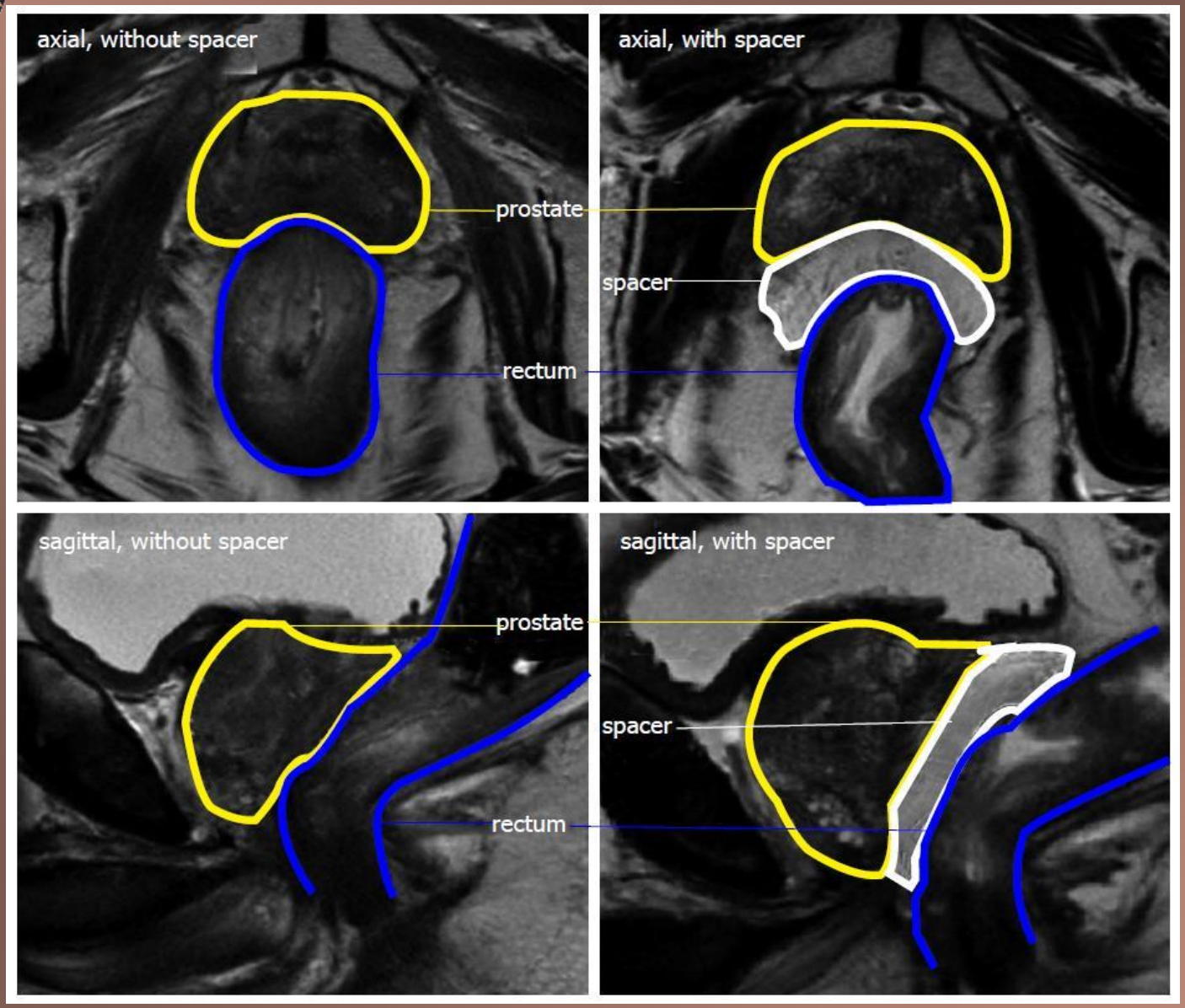
SpaceOAR®



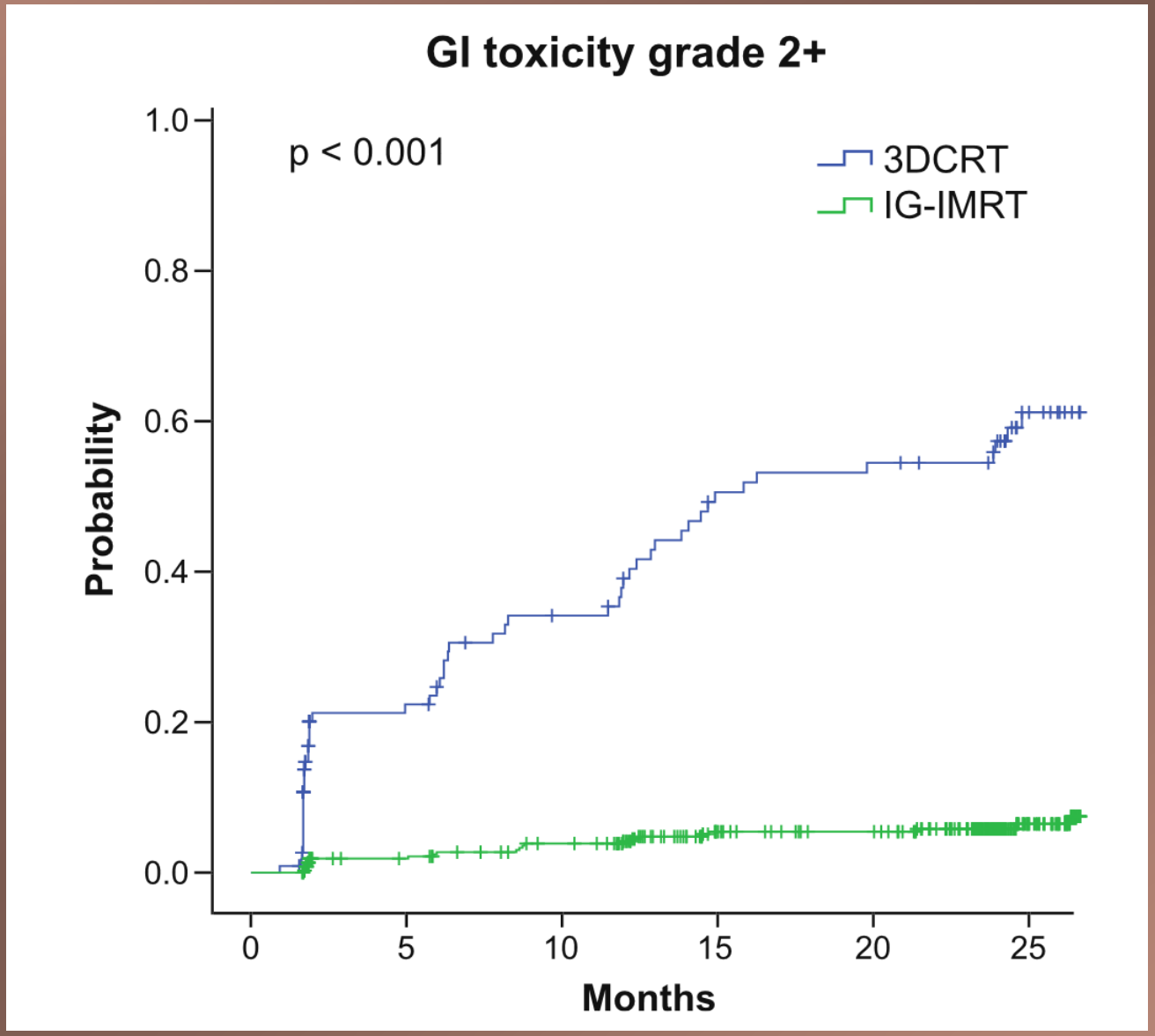
SpaceOAR®


Augmenix
Hydrodissection
and
Application of
SpaceOAR
Inject entire SpaceOAR kit in one continuous motion. Do not stop and start to avoid plugging.

SpaceOAR®


axial, without spacer
prostate
rectum
axial, with spacer
spacer
sagittal, without spacer
prostate
rectum
sagittal, with spacer
spacer

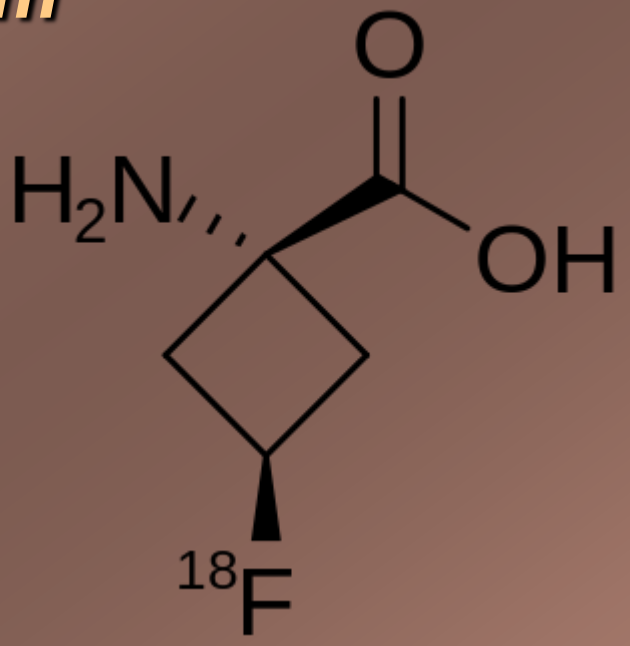
SpaceOAR®


GI toxicity grade 2+
p < 0.001
3DCRT
IG-IMRT
Probability
1.0
0.8
0.6
0.4
0.2
0.0
0
5
10
15
20
25
Months

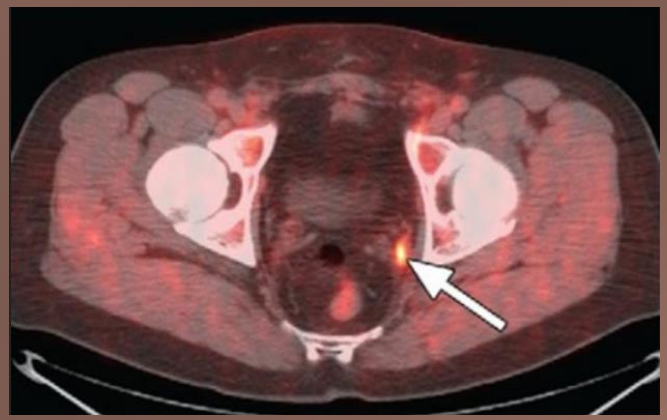
SpaceOAR®

Trial	# Patients	Median F/U	Study Arms	Late Grade 2+ GIToxicity
CHHiP	3216	5.2 years	74 Gy/2 Gy vs 60 Gy 3Gy 57 Gy/3 Gy	14% vs 12%
HYPRO	820	5 years	78 Gy/2 Gy vs 64.6 Gy/3 Gy	18% vs 22%
PROFIT	608	6 years	78 Gy/2 Gy vs. 60 Gy/3 Gy	11% vs 7%
RTOG 0415	1115	5.8 years	73.8 Gy/1.8 Gy vs. 70 Gy/2.5 Gy	14% vs 22%

Axumin™



- Axumin™
- F-18 labeled fluciclovine
- Transported across cell membranes by transporters that are upregulated in prostate cancer cells



^{18}F-Fluciclovine PET/CT for the Detection of Prostate Cancer Relapse

A Comparison to ^{11}C-Choline PET/CT

Cristina Nanni, MD, Riccardo Schiavina, MD,† Eugenio Brunocilla, MD,† Stefano Boschi, PhD,* Marco Borghesi, MD,† Lucia Zanoni, MD,† Cinzia Pettinato, MS,‡ Giuseppe Martorana, MD,† and Stefano Fanti, MD†*

TABLE 5. Local Relapse-Based Analysis

5 LR	^{11}C-Choline (−)	^{11}C-Choline (+)
Fluciclovine (−)	45	0
Fluciclovine (+)	2	3
	$P < 0.0001$	

LR, local relapse.

Axumin^{tm}

- **Advantages:**
- **More sensative than C-11 Choline**
- **Long half-live**
- **Potential use in other malignancies**

Long half-live

Axumin™

FDA U.S. FOOD & DRUG ADMINISTRATION

News & Events

Home > News & Events > Newsroom > Press Announcements

FDA News Release

FDA approves new diagnostic imaging agent to detect recurrent prostate cancer

For Immediate Release May 27, 2016

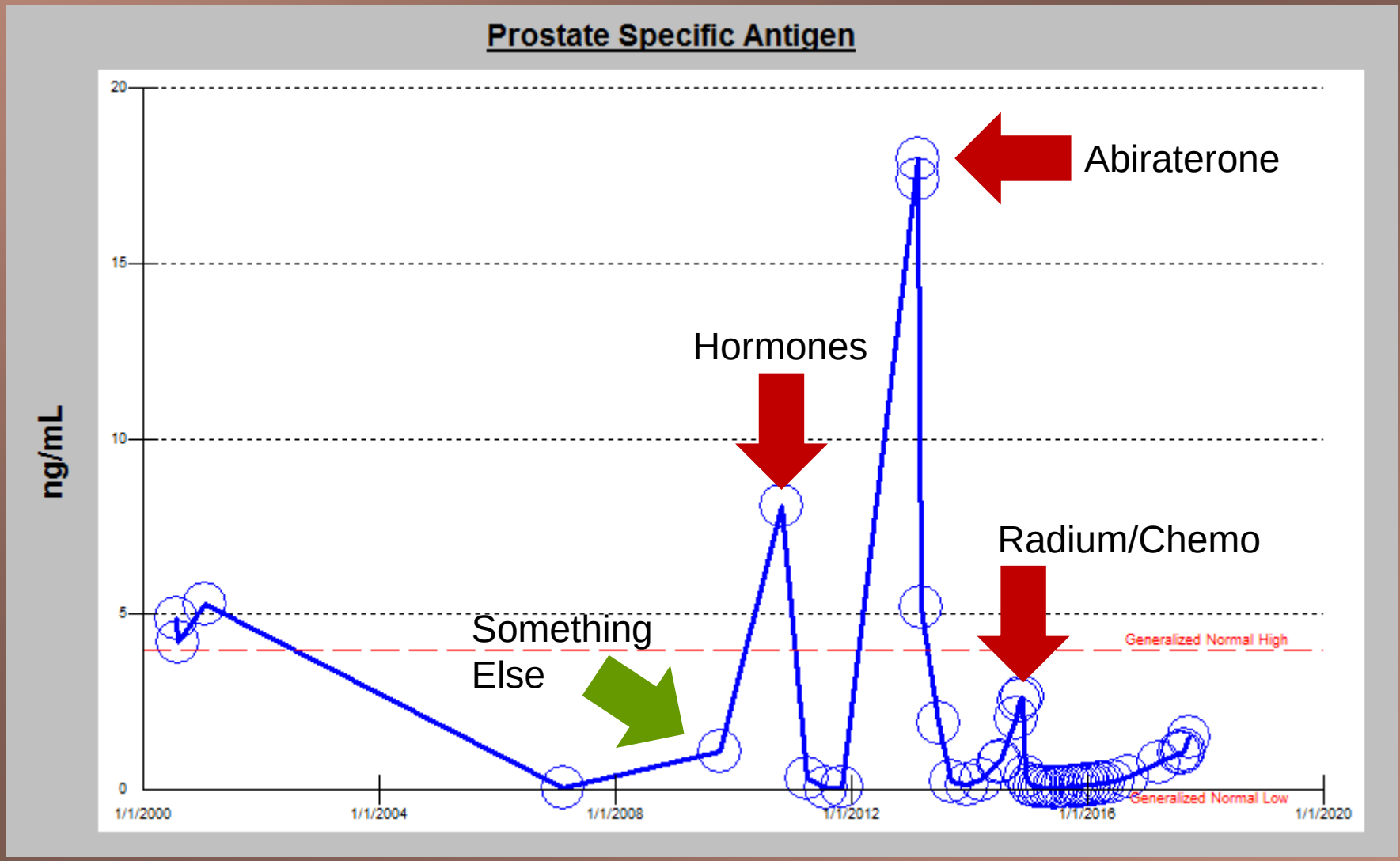
Release

The U.S. Food and Drug Administration today approved Axumin, a radioactive diagnostic agent for injection. Axumin is indicated for positron emission tomography (PET) imaging in men with suspected prostate cancer recurrence based on elevated prostate specific antigen (PSA) levels following prior treatment.

Common Scenario

- 60 y/o male diagnosed with early prostate cancer
- Recieves local therapy (xrt, surgery, …)
- Years later PSA begins to rise

Common Scenario



Oligometastasis

- **Oligo – greek for few, scant**

oligo-

Word Origin

1. a combining form meaning "few," "little," used in the formation of compound words:
oligopoly.

- **Oligometastasis – few metastasis**

Oligometastasis

EDITORIAL

Oligometastases

CANCER TREATMENT is based on an often unstated paradigm of disease pathogenesis. Since 1894, when W.S. Halsted[1,2] clearly elucidated a mechanism of breast cancer spread and used it to design and support the radical mastectomy, surgical and radiotherapeutic approaches to most cancers have been based on this

more about the multistep nature of the development of malignancy.[11-13] Once tumors become invasive, they may gradually acquire the properties necessary for efficient and widespread metastatic spread.[14] Therefore the likelihood, number, and even sites of metastases may reflect the state of tumor development. This suggests that there

Journal of Clinical Oncology, Vol 13, No 1 (January), 1995: pp 8-10

Samuel Hellman
Ralph R. Weichselbaum
The University of Chicago
Chicago, IL

Oligometastasis

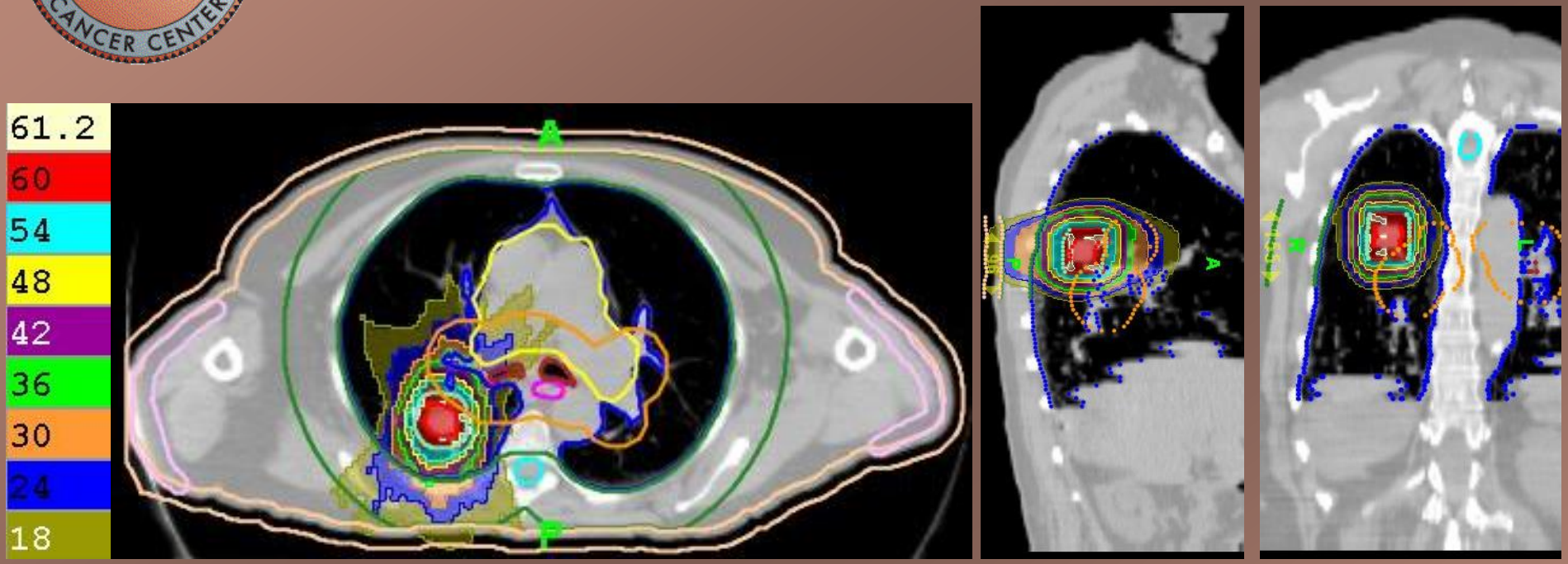
Adenocarcinoma of the kidney with metastasis to the lung cured by nephrectomy and lobectomy

JD Barney, EJ Churchill - J Urol, 1939

Oligometastasis Concepts

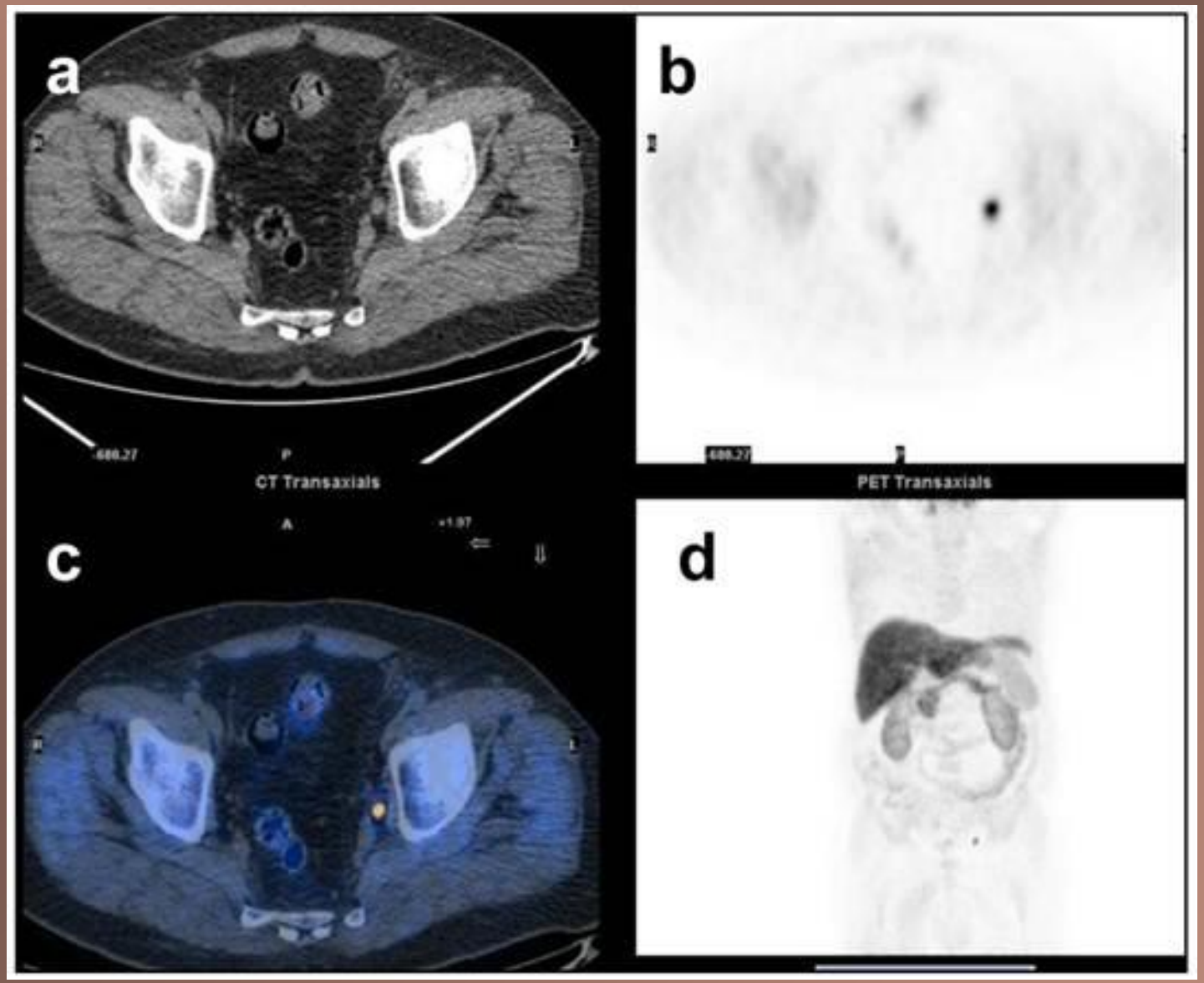
- **There exists a state of a few metastasis where treatment of the metastases could be curable.**
- **Tumors are not monoclonal. Systemic treatments fail because they fail to kill a subset of resistant cells. Local therapies can reduce resistant clones.**
- **Modern imaging can identify smaller metastases. This may facilitate identification of oligometastasis.**

Stereotactic Body Radiotherapy (SBRT)



- **Stereotactic Localization**
- **Organ Motion Management**
- **Strict Patient Immobilization**
- **High Dose per Fraction (1000-2000cGy)**
- **Highly Conformal *Ablative* Dose**

Choline C11 PET-CT



Oligometastasis Data

European Association of Urology

Progression-free Survival Following Stereotactic Body Radiotherapy for Oligometastatic Prostate Cancer Treatment-naive Recurrence: A Multi-institutional Analysis

Piet Ost [a,], Barbara Alicja Jereczek-Fossa [b], Nicholas Van As [c], Thomas Zilli [d], Alexander Muacevic [e], Kenneth Olivier [f], Daniel Henderson [c], Franco Casamassima [g], Roberto Orecchia [b], Alessia Surgo [b], Lindsay Brown [f], Alison Tree [c], Raymond Miralbell [d], Gert De Meerleer [a]*

[a] *Department of Radiotherapy, Ghent University Hospital, Belgium;* [b] *University of Milan and European Institute of Oncology, Milan Italy;* [c] *Department of Radiotherapy Royal Marsden NHS Foundation Trust, London, UK;* [d] *Department of Radiation Oncology, Geneva University Hospital, Geneva, Switzerland;* [e] *Cyberknife Center Munich Grosshadern, Munich, Germany;* [f] *Department of Radiation Oncology, Mayo Clinic, Rochester, MN, USA;* [g] *Ecomedica Radioterapia, Empoli, Italy*

Oligometastasis Data

- Pooled Data from 7 Institutions
- 163 Mets in 119 pts
- ≤ 3 Mets
- DPFS / LPFS
- LPFS 79% ≤ 100Gy
- LPFS 99% > 100Gy
- Median DPFS = 21M

European Association of Urology

Progression-free Survival Following Stereotactic Body Radiotherapy for Oligometastatic Prostate Cancer Treatment-naive Recurrence: A Multi-institutional Analysis

Abstract

The literature on metastasis-directed therapy for oligometastatic prostate cancer (PCa) recurrence consists of small heterogeneous studies. This study aimed to reduce the heterogeneity by pooling individual patient data from different institutions treating oligometastatic PCa recurrence with stereotactic body radiotherapy (SBRT). We focussed on patients who were treatment naive, with the aim of determining if SBRT could delay disease progression. We included patients with three or fewer metastases. The Kaplan-Meier method was used to estimate distant progression-free survival (DPFS) and local progression-free survival (LPFS). Toxicity was scored using the Common Terminology Criteria for Adverse Events. In total, 163 metastases were treated in 119 patients. The median DPFS was 21 mo (95% confidence interval, 15–26 mo). A lower radiotherapy dose predicted a higher local recurrence rate with a 3-yr LPFS of 79% for patients treated with a biologically effective dose ≤100 Gy versus 99% for patients treated with >100 Gy ($p = 0.01$). Seventeen patients (14%) developed toxicity classified as grade 1, and three patients (3%) developed grade 2 toxicity. No grade ≥3 toxicity occurred. These results should serve as a benchmark for future prospective trials.

Patient summary: This multi-institutional study pools all of the available data on the use of stereotactic body radiotherapy for limited prostate cancer metastases. We concluded that this approach is safe and associated with a prolonged treatment progression-free survival.

Oligometastasis Data

European Association of Urology

Progression-free Survival Following Stereotactic Body Radiotherapy for Oligometastatic Prostate Cancer Treatment-naive Recurrence: A Multi-institutional Analysis

Median time from SBRT to ADT: ***28 months*** (95% CI, 16.2–69.7

3-yr DPFS of 31% is comparable with series reporting on oligometastatic recurrences of other primary tumours

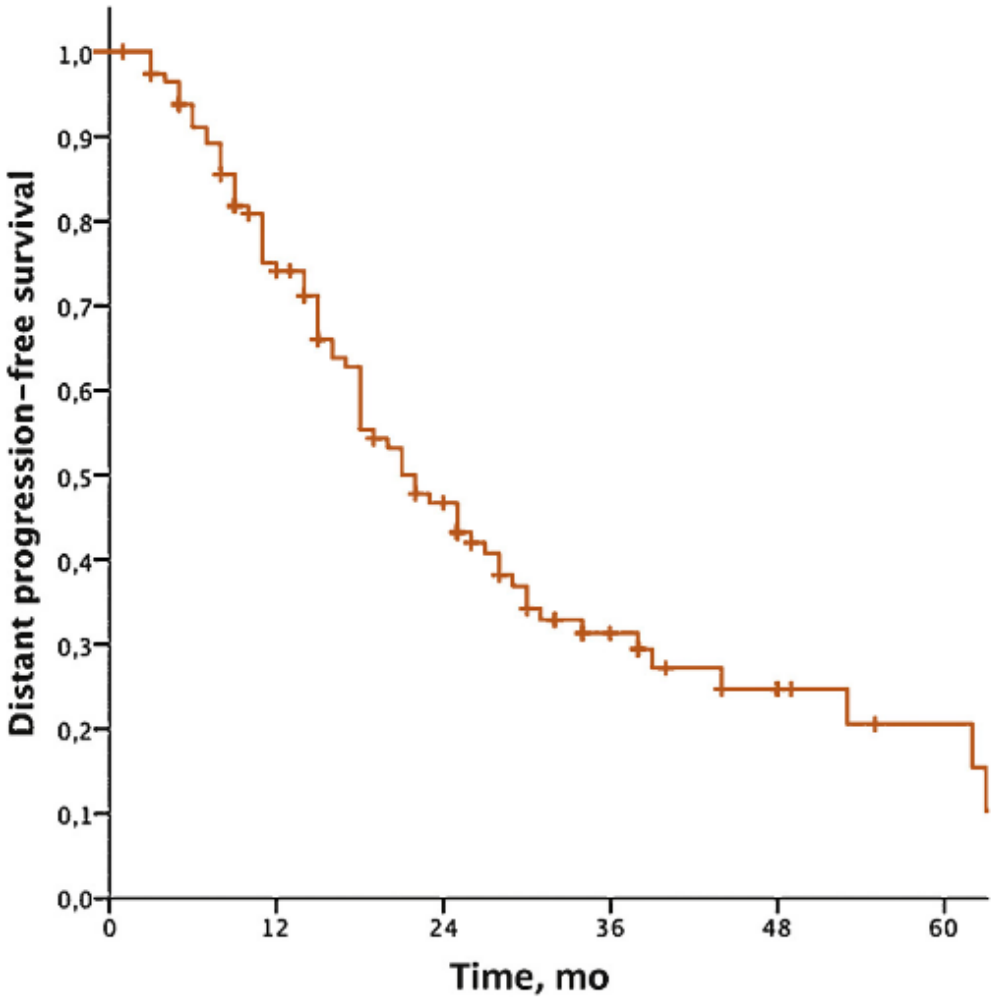


Fig. 1 – Kaplan-Meier analysis depicting time to distant progression.

Oligometastasis Data

Radiat Oncol. 2016 Jan 22;11(1):9. doi: 10.1186/s13014-016-0586-x.

[(18)F]Choline PET/CT and stereotactic body radiotherapy on treatment decision making of oligometastatic prostate cancer patients: preliminary results.

Pasqualetti F[1,2], Panichi M[3], Sainato A[4], Matteucci F[5], Galli L[6], Cocuzza P[7], Ferrazza P[8], Coraggio G[9], Pasqualetti G[10], Derosa L[11], Sollini M[12], Mannelli L[13], Ortori S[14], Monzani F[15], Ricci S[16], Greco C[17], Fabrini MG[18], Erba PA[19].

⊕ Author information

Abstract

BACKGROUND: A new entity of patients with recurrent prostate cancer limited to a small number of active metastatic lesions is having growing interest: the oligometastatic patients. Patients with oligometastatic disease could eventually be managed by treating all the active lesions with local therapy, i.e. either surgery or ablative stereotactic body radiotherapy. This study aims to assess the impact of [(18)F]Choline ([(18)F]FMCH) PET/CT and the use stereotactic body radiotherapy (SBRT) in patients (pts) with oligometastatic prostate cancer (PCa).

METHODS: Twenty-nine pts with oligometastatic PCa (≤3 synchronous active lesions detected with [(18)F]FMCHPET/CT) were treated with repeated salvage SBRT until disease progression (development of > three active synchronous metastases). Primary endpoint was systemic therapy-free survival measured from the baseline [(18)F]FMCHPET/CT.

RESULTS: A total of 45 lesions were treated with SBRT. After a median follow-up of 11.5 months (range 3-40 months), 20 pts were still in the study and did not receive any systemic therapy. Nine pts started systemic therapy, and the median time of the primary endpoint was 39.7 months (CI 12.20-62.14 months). No grade 3 or 4 toxicity was recorded.

CONCLUSIONS: Repeated salvage [(18)F]FMCHPET/CT-guided SBRT is well tolerated and could defer the beginning of systemic therapy in selected patients with oligometastatic PCa.

Oligometastasis Data

Clin Transl Oncol. 2015 Oct 19. [Epub ahead of print]

Stereotactic body radiation therapy (SBRT) delays the emergence of castration resistance in patients with oligometastatic prostate cancer.

Martínez-Fernández MI[1,2], Pérez Gracia JL[3,4], Gil-Bazo I[3,4], Martínez-Monge R[3,4].

⊕ Author information

Abstract

PURPOSE: To investigate whether bon e metastases-directed stereotactic body radiation therapy (SBRT) delays the emergence of castration resistance in patients with oligometastatic prostate cancer (OPC).

METHODS AND MATERIAL: OPC is usually managed with androgen deprivation therapy (ADT). Migration to castration-resistant prostate cancer will inevitably occur in the majority of these patients. There are several strategies aimed to delay the emergence of castration resistance including intermittent ADT, second generation antiandrogens (abiraterone, enzalutamide) or metastases-directed SBRT. The present report describes two cases of patients with OPC that received SBRT 24 Gy/3Rx to the solitary bony lesion after ADT failure.

RESULTS: Both cases showed complete and durable biochemical response for 13 and 17 months, respectively.

CONCLUSIONS: SBRT can be used to delay the emergence of castration resistance and the need for systemic therapy when used after ADT failure.

Oligometastasis Data

Table 1 – Full-text publications of metastasis-directed therapy for oligometastatic prostate cancer recurrence included in the systematic review

Study	No. of patients	Site of metastasis: node/bone/visceral	Median time to metastatic recurrence, mo	Median PSA at time of metastasis	Staging method	Type of MDT	Median follow-up, mo	Median PFS	Adjuvant ADT (%)	Median duration ADT	Prophylactic nodal radiotherapy (%)
Casamassima et al. [23]	25	25/0/0	11.8–36.7	5.65	Choline PET/CT	SBRT	29	24 mo	None	NA	7 (28)
Muacevic et al. [24]	40	0/40/0	NR	5.4	Choline PET/CT	SBRT	14*	NR	27 (68)	NR	NA
Würschmidt et al. [25]	15	15/0/0	NR	1.79	Choline PET/CT	NRT	28	Median not reached: 3-yr PFS: 75%	NR	NR	15 (100)
Ahmed et al. [26]	17	1/15/1	50.4	2.1	Choline PET/CT ($n = 9$), MRI ($n = 6$), CT ($n = 1$), and biopsy ($n = 1$)	SBRT	6	12 mo	15 (88)	NR	NA
Jereczek-Fossa et al. [27]	19	18/1/0	66	1.77 (pelvic nodes); 10.7 (M1)	Choline PET/CT	SBRT	17	Median not reached; 30-mo PFS: 63.5%	19 (100)	12–17 mo	None
Schick et al. [28]	50	33/15/2	15.6	6.7	Choline PET/CT and bone scintigraphy	SBRT ($n = 14$) NRT ($n = 36$)	31	Median not reached; 3-yr PFS: 58.6%	49 (98)	12 mo	25 (50)
Decaestecker et al. [29]	50	27/22/1	57.6	3.8	Choline ($n = 18$) or FDG ($n = 32$) PET/CT	SBRT	25	19 mo	35 (70)	1 mo	None
Picchio et al. [30]	83	83/0/0	NR	2.6	Choline PET/CT	HRT	22	NR	58 (70)	NR	77 (93)
Rinnab et al. [31]	15	15/0/0	NR	1.98	Choline PET/CT	LND	13.7*	NR	11 (73)	NR	1 (7)
Schilling et al. [32]	10	10/0/0	NR	8.75	Choline PET/CT	LND	11*	NR	6 (60)	NR	None
Winter et al. [33]	6	6/0/0	NR	2.04	Choline PET/CT	LND	24 mo	NR	None	NA	None
Busch et al. [37]	6	6/0/0	Mean: 79.9	37.6*	Choline ($n = 3$), MRI ($n = 1$), CT ($n = 2$)	LND	NR	15.5 mo	6 (100)	Lifelong ADT	None
Jilg et al. [34]	47	47/0/0	62	11.1*	Choline PET/CT	LND	35.5	27 mo**	34 (65)	NR	27 (52)
Martini et al. [35]	8	8/0/0	NR	1.62	Choline PET/CT	LND	NR	NR	None	NA	None
Suardi et al. [36]	59	59/0/0	NR	2.0	Choline PET/CT	LND	76.6	60 mo**	24 (41)	24 mo	21 (36)

ADT = androgen-deprivation therapy; CT = computed tomography; FDG = fluorodeoxyglucose; HRT = hypofractionated radiotherapy; LND = lymph node dissection; MDT = metastasis-directed therapy; MRI = magnetic resonance imaging; NA = not applicable; NR = not reported; NRT = normofractionated radiotherapy; PET/CT = positron emission tomography with coregistered computed tomography; PFS = progression-free survival; PSA = prostate-specific antigen; SBRT = stereotactic body radiotherapy.

* Mean numbers reported instead of median.

** Median estimated from curves.

Current Studies in O-Mets

Surveillance or metastasis-directed Therapy for OligoMetastatic Prostate cancer recurrence (STOMP): study protocol for a randomized phase II trial

Karel Decaestecker, Gert De Meerleer, Filip Ameye, Valerie Fonteyne, Bieke Lambert, Steven Joniau, Louke Delrue, Ignace Billiet, Wim Duthoy, Sarah Junius, Wouter Huysse, Nicolaas Lumen and Piet Ost

Background

Metastases-directed therapy (MDT) with surgery or stereotactic body radiotherapy (SBRT) is emerging as a new treatment option for prostate cancer (PCa) patients with a limited number of metastases (≤3) at recurrence – so called "oligometastases". One of the goals of this approach is to delay the start of palliative androgen deprivation therapy (ADT), with its negative impact on quality of life. However, the lack of a control group, selection bias and the use of adjuvant androgen deprivation therapy prevent strong conclusions from published studies.

Current Studies in O-Mets

NRG-BR001: A Phase 1 Study of Stereotactic Body Radiotherapy (SBRT) for the Treatment of Multiple Metastases

NRG-BR001PowerPoint Presentation

NRG ONCOLOGY

Advancing Research. Improving Lives.™

Principal Investigator

Steven Chmura, MD

Primary Objective

To determine the recommended SBRT dose for each of the metastatic locations being treated given the individual and overlapping fields when multiple metastases are treated with SBRT in a national clinical trials network setting

Patient Population

Oligometastases arising from the breast, lung or prostate; oligometastases defined as ≤ 4 distinct metastases visualized on standard imaging studies; all metastases not resected must be amenable to SBRT; local and regional disease treated per standard of care with no evidence of progression

Presenting with Metastasis

Oncology

A Pilot Study of a Multimodal Treatment Paradigm to Accelerate Drug Evaluations in Early-stage Metastatic Prostate Cancer

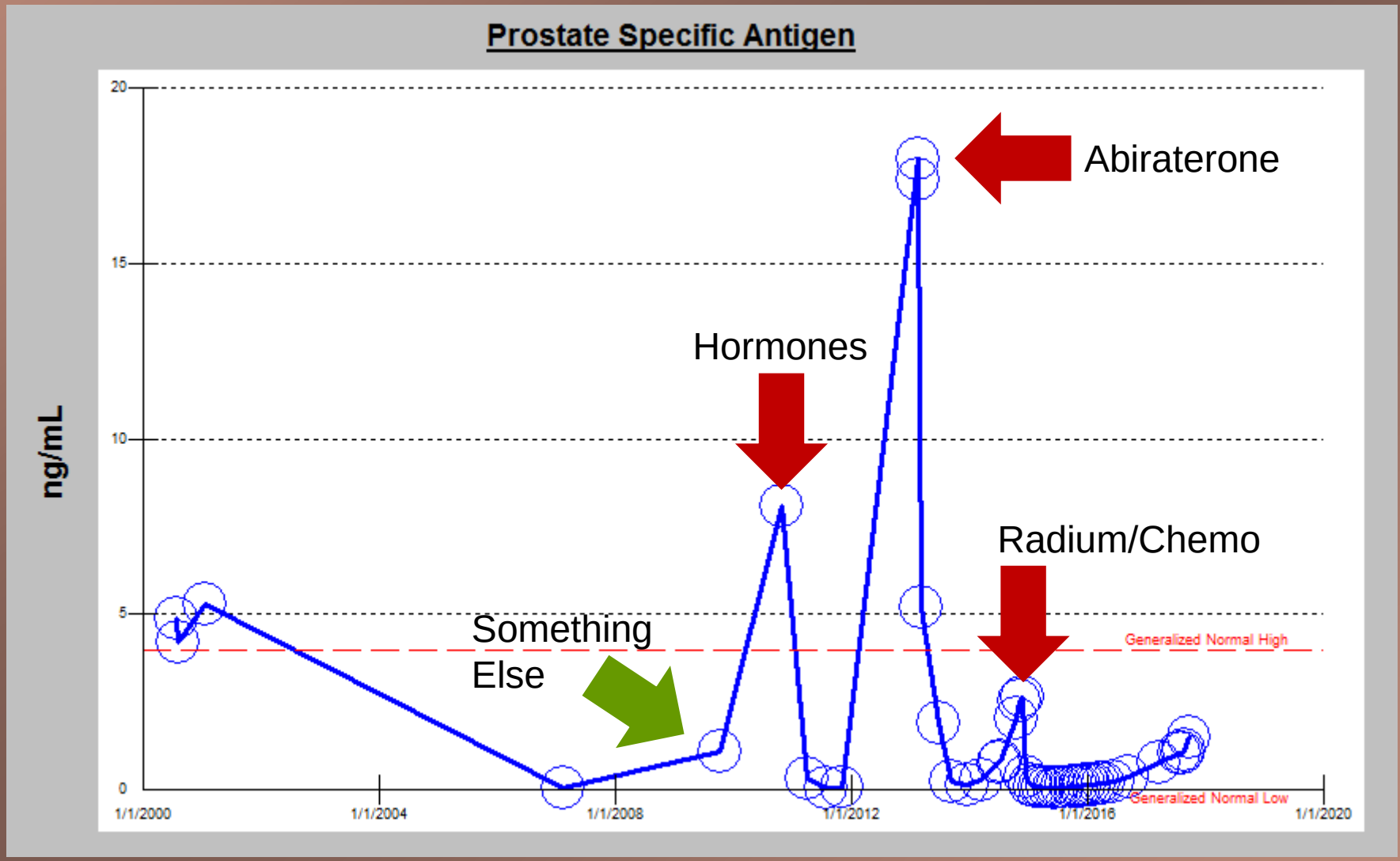
Matthew J. O'Shaughnessy, Sean M. McBride, Hebert Alberto Vargas, Karim A. Touijer, Michael J. Morris, Daniel C. Danila, Vincent P. Laudone, Bernard H. Bochner, Joel Sheinfeld, Erica S. Dayan, Lawrence P. Bellomo, Daniel D. Sjoberg, Glenn Heller, Michael J. Zelefsky, James A. Eastham, Peter T. Scardino, and Howard I. Scher

- 20 Patients
- All had mets
- Surgery, SBRT, ADT for 1 year
- 27% with bone mets had undetectable PSA with normal testosterone level

- **1 patient went 4 years with normal testosterone and undetectable PSA**

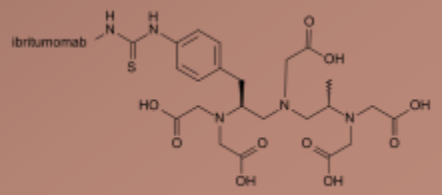
UROLOGY 102, 2017

Common Scenario



Wild Speculation

- **Fluciclovine is one agent of many in development**
- **If these molecules become very specific for cancer**
- **Could we tag these agents with chemotherapy or stronger radioactive elements – image and treat at the same time. (Zevalin - Ibritumomab tiuxetan)**




Questions?