Pet Choline
Guided Salvage Radiatin Therapy

G.Beltramo

Centro Diagnostico Italiano - Milano

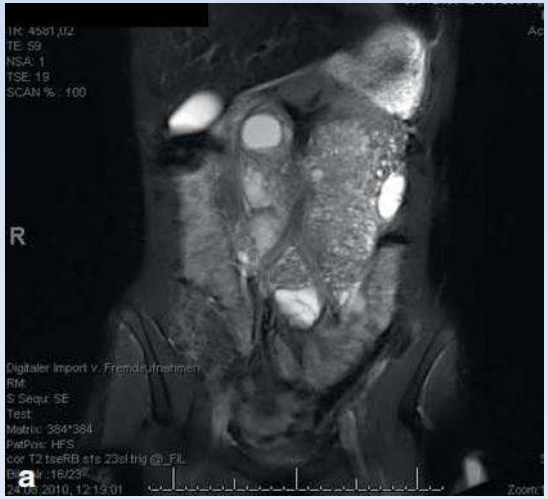
2° UROLOGY FORUM, 15 – 16 MAY 2015, ATHENS

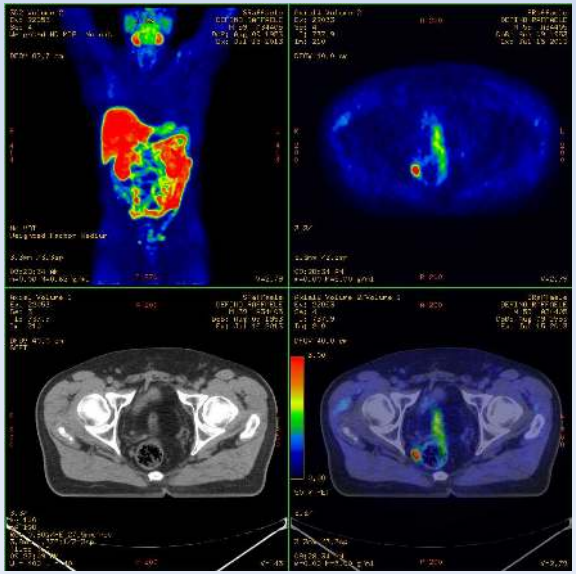
role of imaging in recurrent prostate cancer

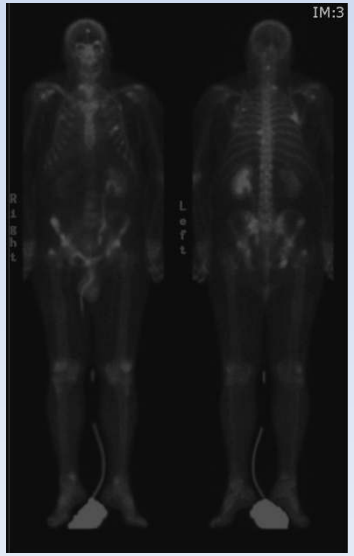
Imaging in prostate cancer Would have clinical utility only if it is able to :

1) Preoperatively identify extra prostatic extension and thereby impact the decision on local radical therapy

2) Accurately detect relapse/recurrence following local radical therapy







Management of urological malignancies:has positron emission tomography/computed tomography made a difference ?

- PET/CT integrates both functional and anatomical imaging
- In recent years, there have been improvements in hardware, software and radiopharmaceutical that contributed to the improvement of this technique

Tracer	Half-life	Mechanism
18F-FDG	110 min	Glucose metabolism
11C / 18F Choline	**20 / 110 min**	**Phosfolipid synthesis, choline kinase upregulated in tumors**
11C-Acetate	20 min	Fatty acid and cholesterol synthesis
18F-NaF	110 min	Osteoblastic activity in bones
18F-FACBC	110 min	L-leucine analog, aminoacid transport
68Ga-PSMA	68 min	Targeting of Prostate Specific Membrane Antigen

The Role of 11C-Choline and 18F-Fluorocholine Positron Emission Tomography (PET) and PET/CT in Prostate Cancer: A Systematic Review and Meta-analysis

Martin H. Umbehr[a,b,], Michael Müntener[c], Thomas Hany[d], Tullio Sulser[b], Lucas M. Bachmann[a]*

Clinical impact of ^{18}F-choline PET/CT in patients with recurrent prostate cancer

Jan D. Soyka · Marco A. Muster · Daniel T. Schmid · Burkhardt Seifert · Ulrike Schick · Raymond Miralbell · Sandra Jorcano · Kathrin Zaugg · Hans-Helge Seifert · Patrick Veit-Haibach · Klaus Strobel · Niklaus G. Schaefer · Daniela B. Husarik · Thomas F. Hany

	SENSITIVITY	PRIMARY TREATMENT	HISTOLOGICAL EVALUATION	RESPONSE
Picchio et al	55%	RP	No	Conventional imaging
Reske et al	73%	RP	Yes	Histological evaluation + response to salvage RT
Vees et al	50% (PSA<1)	RP	No	MRI and response to salvage RT
Souvatzoglou et al	30%	RP	No	Conventional imaging
Panebianco et al	62%	RP	Yes	Histological evaluation +MRI

PET/CT is not recommended for detection of local recurrence after radical prostatectomy, because the sensitivity of PET/CT is very low

Eur J Nucl Med Mol Imaging (2012 39: 936-943)

CLINICAL INVESTIGATION **Prostate**

DETECTION OF LOCAL, REGIONAL, AND DISTANT RECURRENCE IN PATIENTS WITH PSA RELAPSE AFTER EXTERNAL-BEAM RADIOTHERAPY USING ^{11}C-CHOLINE POSITRON EMISSION TOMOGRAPHY

ANTHONIUS J. BREEUWSMA,*† JAN PRUIM, PH.D.,† ALPHONS C. M. VAN DEN BERGH, PH.D.,‡ ANNA M. LELIVELD,* RIEN J. M. NIJMAN, PH.D.,* RUDI A. J. O. DIERCKX, PH.D.,† AND IGLE J. DE JONG, PH.D.*

	per-pt based 12 studies, 1055 pts
Sensitivity	85% (95% CI, 89-89%)
Specificity	88% (95% CI, 73-95%)
DOR	41.4 (95% CI, 19.7-86.8)

	N. pts	PSA	Choline Isotope	Positive DR
Vees et al. 2007	11	< 1 ng/mL	[18F]	45%
Krause et al. 2008	63	< 1 ng/mL	[11C]	36%
Giovacchini et al. 2010	141	< 1 ng/mL	[11C]	19%
Castellucci et al. 2011	102	< 1.5 ng/mL	[11C]	28%
Giovacchini et al. 2013	75	< 1.5 ng/mL	[11C]	21%

Promising for local recurrence after RT

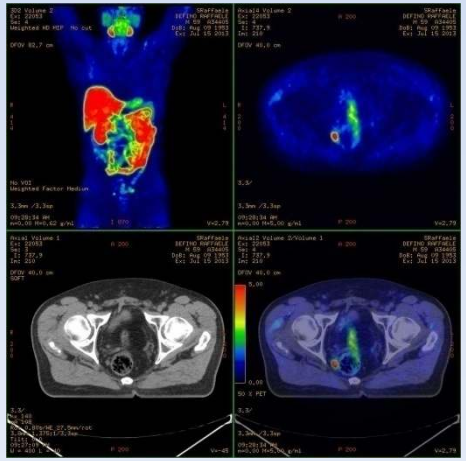
Clinical Recommendation

- 11-c choline PET/CT when PSA > 1 ng/ml

Int. J. Radiation Oncology Biol. Phys., Vol. 77, 2010

Detection of Lymph-Node Metastases with Integrated [^{11}C]Choline PET/CT in Patients with PSA Failure after Radical Retropubic Prostatectomy: Results Confirmed by Open Pelvic-Retroperitoneal Lymphadenectomy

Parameter	Per patient (n = 25)	Per lesion (n = 63)					
		Overall (n = 63)	PSA < 2.0 ng/ml (n = 32)	PSA ≥ 2.0 ng/ml (n = 31)	Retroperitoneum (n = 13)	Right pelvic (n = 25)	Left pelvic (n = 25)
Sensitivity (%)	100%	64%	64%	62%	80%	54%	60%
Specificity (%)	66%	90%	85%	100%	100%	92%	86%
PPV (%)	90%	86%	70%	100%	100%	85%	75%
NPV (%)	100%	72%	82%	55%	60%	72%	76%
Accuracy (%)	92%	77%	78%	74%	84%	76%	76%



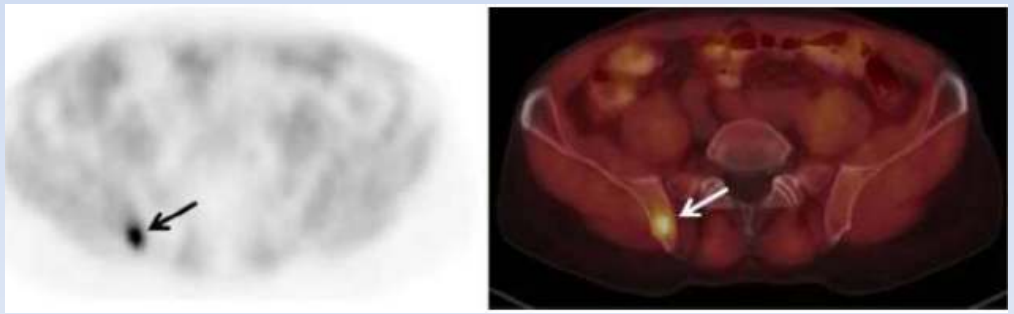
- PET/CT is useful for indicating the presence of nodal recurrence
- Can miss micro (< 5 mm) metastatic Lymph node

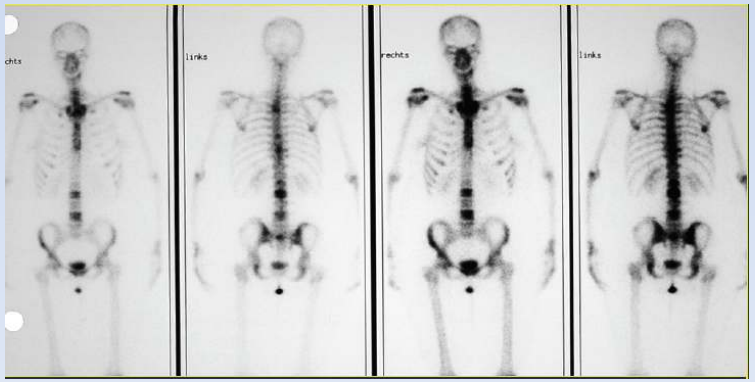
Scattoni V et al:Eur Urol 2007; 53:423-9

[^{11}C]Choline PET/CT detection of bone metastases in patients with PSA progression after primary treatment for prostate cancer: comparison with bone scintigraphy

Maria Picchio · Elena Giulia Spinapolice · Federico Fallanca · Cinzia Crivellaro · Giampiero Giovacchini · Luigi Gianolli · Cristina Messa

	[^{11}C]Choline PET/CT		BS	
	EQ result pos.	EQ result neg.	EQ result pos.	EQ result neg.
Sensitivity	89%	89%	100%	70%
Specificity	98%	100%	75%	100%
PPV	96%	100%	68%	100%
NPV	94%	96%	100%	86%
Accuracy	95%	96%	83%	90%





Choline PET/CT exhibits a lower sensitivity but higher specificity and PPV than BONE SCAN in the diagnosis of bone lesions

Eur J Nucl Med Mol Imaging (2012 39: 13-26

Radiotherapy and Oncology 99 (2011) 193–200

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

^{11}C Choline- PET in prostate RT

Influence of ^{11}C-choline PET/CT on the treatment planning for salvage radiation therapy in patients with biochemical recurrence of prostate cancer

Michael Souvatzoglou [a,*], Bernd J. Krause [a], Anja Pürschel [b], Reinhard Thamm [b], Tibor Schuster [c], Andreas K. Buck [a], Frank Zimmermann [b], Michael Molls [b], Markus Schwaiger [a], Hans Geinitz [b]

Radiotherapy and Oncology 96 (2010) 347–350

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review

Clinical evidence on PET/CT for radiation therapy planning in prostate cancer

Maria Picchio [a,b,*], Elisabetta Giovannini [a], Cinzia Crivellaro [b], Luigi Gianolli [a], Nadia di Muzio [c], Cristina Messa [b,d,e]

NOVEL SCENARIO in treatment of prostate cancer recurrence to image guided targeted approach

Study	No. of patients	Site of metastasis: node/bone/visceral	Median PSA at time of metastasis	Staging method	Type of MDT	Median follow-up, mo	Median PFS
Casamassima et al. [23]	25	25/0/0	5.65	Choline PET/CT	SBRT	29	24 mo
Muacevic et al. [24]	40	0/40/0	5.4	Choline PET/CT	SBRT	14*	NR
Würschmidt et al. [25]	15	15/0/0	1.79	Choline PET/CT	NRT	28	Median not reached: 3-yr PFS: 75%
Ahmed et al. [26]	17	1/15/1	2.1	Choline PET/CT (n = 9), MRI (n = 6), CT (n = 1), and biopsy (n = 1)	SBRT	6	12 mo
Jereczek-Fossa et al. [27]	19	18/1/0	1.77 (pelvic nodes); 10.7 (M1)	Choline PET/CT	SBRT	17	Median not reached 30-mo PFS: 63.5%
Schick et al. [28]	50	33/15/2	6.7	Choline PET/CT and bone scintigraphy	SBRT (n = 14) NRT (n = 36)	31	Median not reached 3-yr PFS: 58.6%
Decaestecker et al. [29]	50	27/22/1	3.8	Choline (n = 18) or FDG (n = 32) PET/CT	SBRT	25	19 mo
Picchio et al. [30]	83	83/0/0	2.6	Choline PET/CT	HRT	22	NR
Rinnab et al. [31]	15	15/0/0	1.98	Choline PET/CT	LND	13.7*	NR
Schilling et al. [32]	10	10/0/0	8.75	Choline PET/CT	LND	11*	NR
Winter et al. [33]	6	6/0/0	2.04	Choline PET/CT	LND	24 mo	NR
Busch et al. [37]	6	6/0/0	37.6*	Choline (n = 3), MRI (n = 1), CT (n = 2)	LND	NR	15.5 mo
Jilg et al. [34]	47	47/0/0	11.1*	Choline PET/CT	LND	35.5	27 mo**
Martini et al. [35]	8	8/0/0	1.62	Choline PET/CT	LND	NR	NR
Suardi et al. [36]	59	59/0/0	2.0	Choline PET/CT	LND	76.6	60 mo**

True-Beam

Rapid Arc

Cyber Knife

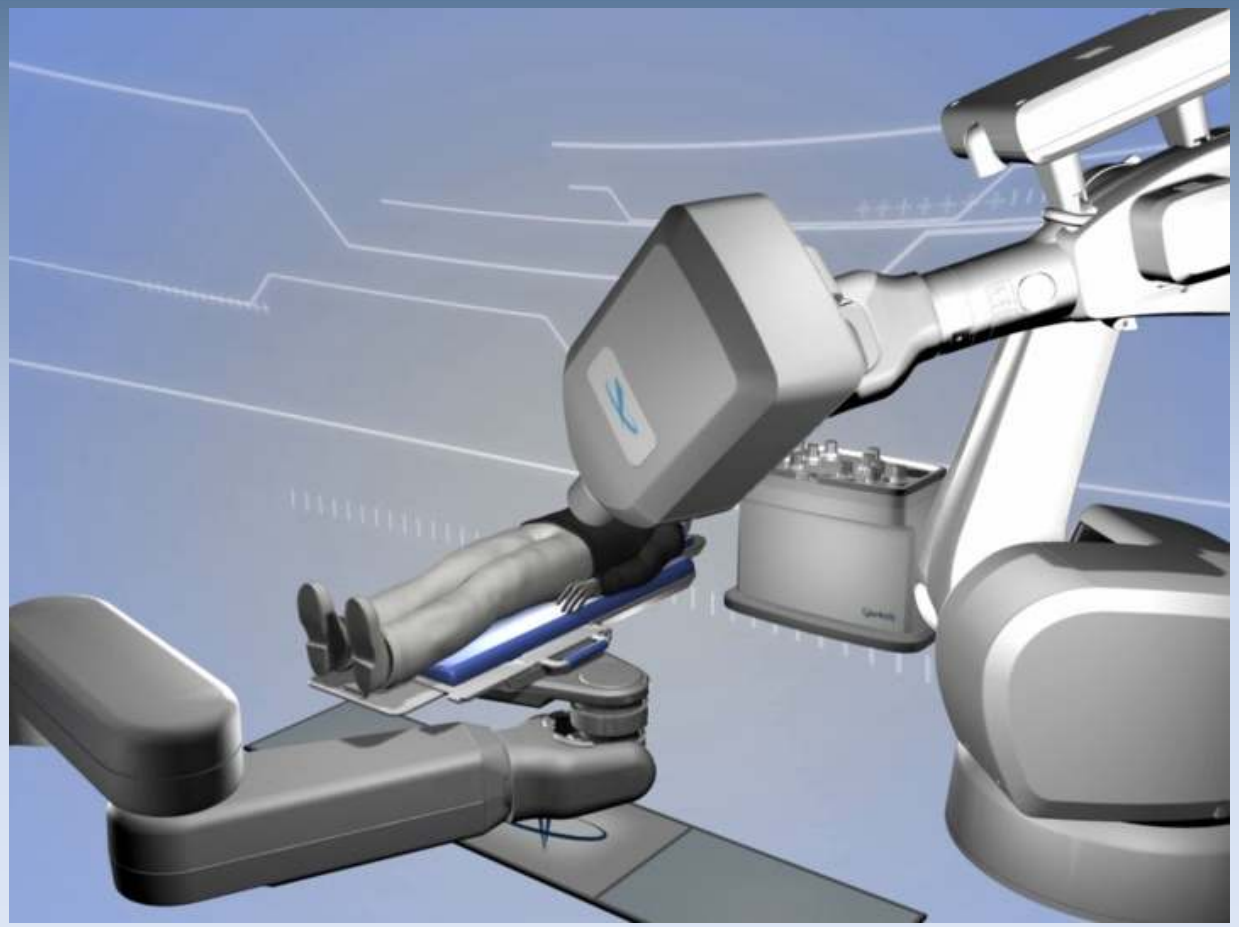
Advanced in Technology: recent IMRT available Machines

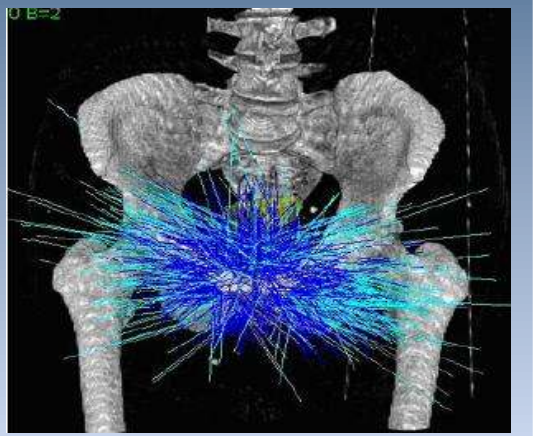
VMAT

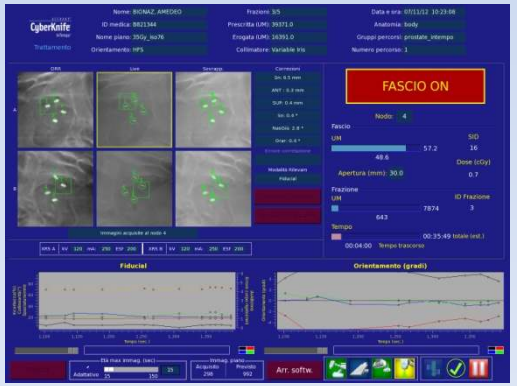
Helical Tomo therapy

Serial Tomo therapy

Verification of treatment accuracy







Accuracy of radiotherapy delivery depends on the Neoplastic Target at the time of treatment and comparison with references images obteined during treatment planning, . The advantage of Cyberknife tracking sistem is to verify in every step of treatment the real position of neoplstic target and the possibility to adjust the aim of robotic arm if the target position change during radiotherapy treatment

Image – guided Robotic Radiosurgery treatment as salvage therapy for locally recurrent prostate cancer following EBRT

September 2007 - August 2013 : 59 patients

- **Initial stage according to NCCC:**

low	14
intermedie	12
high	33

- **EBRT Median Dose: 76 Gy (Range 70-80 Gy)**

- **The work-up included PSA detection, bone scan, abdominal-pelvic CT, MRI, and CT/PET scan using C-11 choline.**

- **The median time to failure was 84 months (range 18 -120.6 months).**

- **The median age of the patients at the time of CK was 70 years (range 56-82 years)**

CLINICAL INVESTIGATION **Genitourinary Cancer**

ROBOTIC IMAGE-GUIDED STEREOTACTIC RADIOTHERAPY, FOR ISOLATED RECURRENT PRIMARY, LYMPH NODE OR METASTATIC PROSTATE CANCER

BARBARA ALICJA JERECZEK-FOSSA, M.D., PH.D.,*† GIANCARLO BELTRAMO, M.D.,‡ LAURA FARISELLI, M.D.,§ CRISTIANA FODOR, M.SC.,* LUIGI SANTORO, M.SC.,‖ ANDREA VAVASSORI, M.D.,* DARIO ZERINI, M.D.,* FEDERICA GHERARDI, M.D.,*† CARMEN ASCIONE, M.D.,*¶ ISA BOSSI-ZANETTI, M.D.,*† ROBERTA MAURO, M.D.,*† ACHILLE BREGANTIN, M.SC.,‡ LIVIA CORINNA BIANCHI, M.D.,‡ OTTAVIO DE COBELLI, M.D.,# AND ROBERTO ORECCHIA, M.D.*†

Departments of *Radiotherapy, #Urology, and ‖Epidemiology and Statistics, European Institute of Oncology, Milan, Italy; †University of Milan, Milan, Italy; ‡CyberKnife Center CDI, Milan, Italy; §Radiotherapy Unit, Carlo Besta Neurological Institute Foundation, Milan, Italy; and ¶Seconda Università degli Studi di Napoli, Naples, Italy

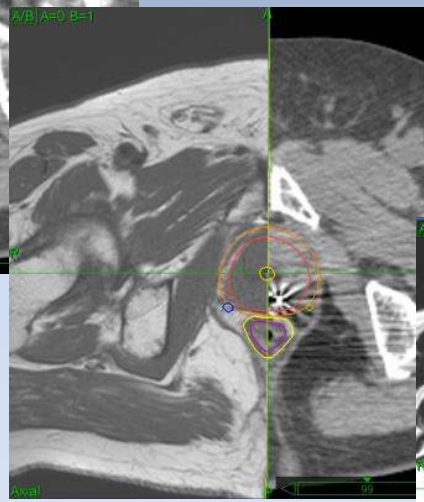
Table 2. Patient and CBK-SRT treatment characteristics (n = 34 patients/38 lesions)

Characteristics	P (n = 15)	A (n = 4)	LN (n = 16)	M (n = 3)	All lesions (n = 38)
Pre–CBK-SRT PSA [median (range)] (ng/mL)	3.51 (1.69 – 22.9)	6.60 (0.47 – 10.11)	1.77 (0.22 – 15.50)	10.7 (0.30 – 38.3)	3.20 (0.22 – 38.3)
[^{11}C]choline PET/CT before CBK-SRT					
Yes	13 (87%)	2 (50%)	16 (100%)	3 (100%)	34 (89%)
No	2 (13%)	2 (50%)	0	0	4 (11%)
Biopsy of target lesion					
Yes	15 (100%)	3 (75%)	1 (6%)	0	19 (50%)
No	0	1 (25%)	15 (94%)	3 (100%)	19 (50%)
Fiducial marker in target lesion					
Yes	14 (93%)	3 (75%)	9 (56%)	0	26 (68%)
No	1 (7%)	1 (25%)	7 (44%)	3 (100%)	12 (32%)
Localization in previous RT volume					
Yes	15 (100%)	4 (100%)	8 (50%)	0	27 (71%)
No	0	0	8 (50%)	3 (100%)	11 (29%)
Lymph node site (only LN group)					
External iliac			5 (31%)		
Internal iliac			0		
Common iliac			3 (19%)		
Pararectal			1 (6%)		
Obturator			7 (44%)		

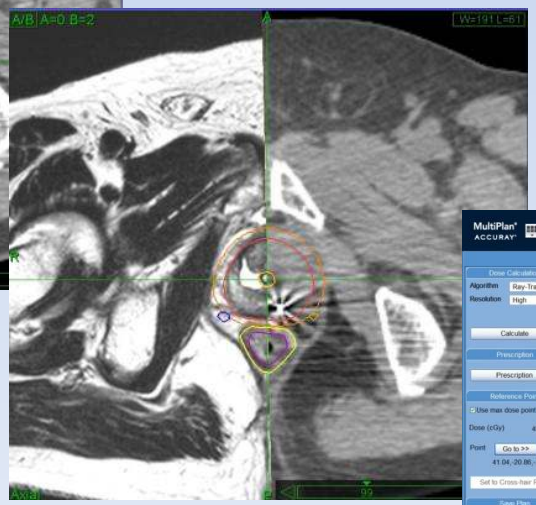
Int. J. Radiation Oncology Biol. Phys., Vol. 82, 2012

Image guidance facilitates targetting

TC

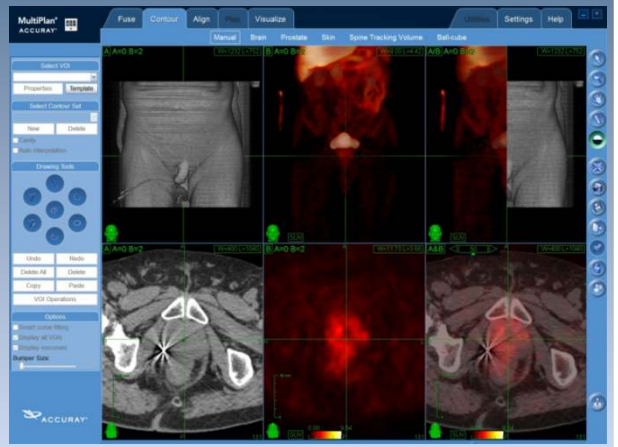


T1 MR1



T2 MRI

TC-MRI-PET image Fusion

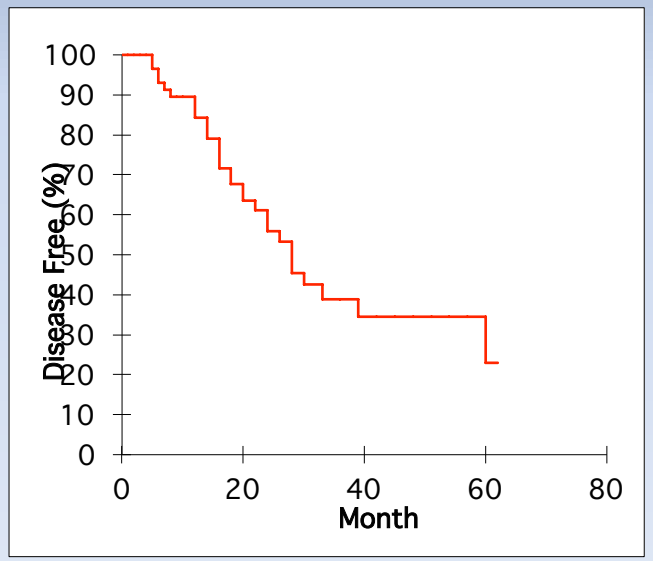


Use CT for geometric accuracy
Use MRI – CT/PET for target delineation

Image – guided Robotic Radiosurgery treatment as salvage therapy for locally recurrent prostate cancer following EBRT

September 2007 - August 2013 : 59 patients

Median follow up: 41 months (range 33-84)



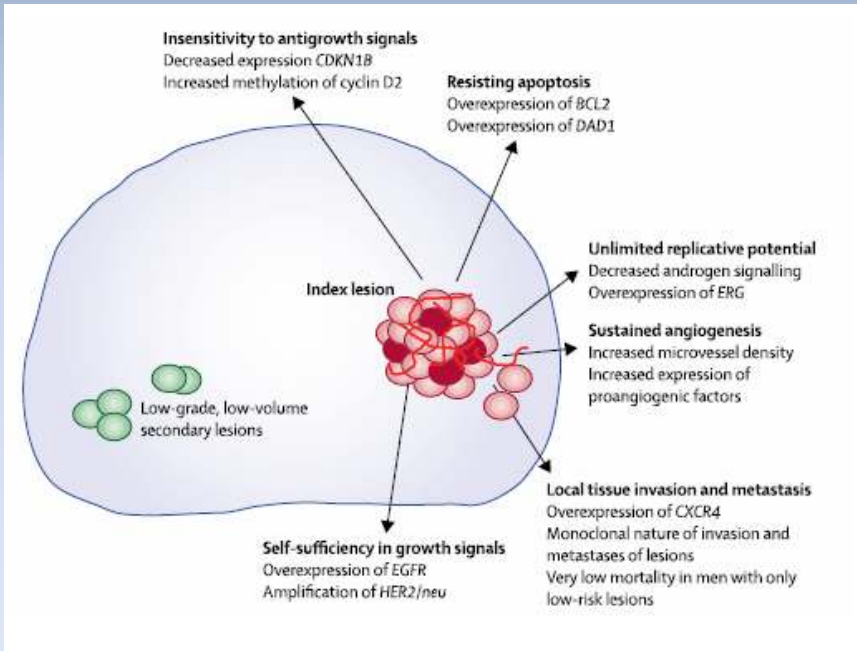
Treatment regimen consisted of 5 fractions of 6-7 Gy for a total dose of 30-35 Gy

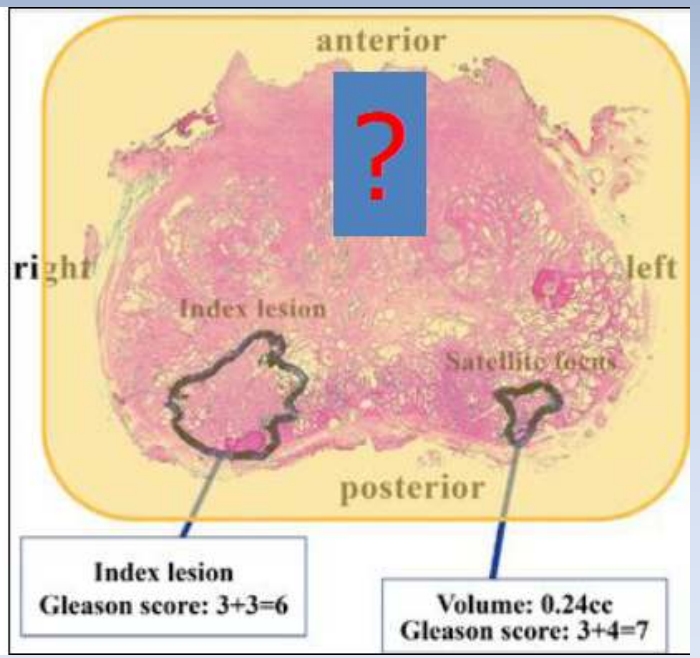
The actuarial psa relapse free survival rate is 84.2 % (CI: 75.0%-93%) at the first years and 56% (CI: 34.0%-86%) at the second years respectively..

Do low-grade and low-volume prostate cancers bear the hallmarks of malignancy?

Hashim Uddin Ahmed, Manit Arya, Alex Freeman, Mark Emberton

Prostate cancer is generally multifocal and consists of a dominant focus—measured by tumour volume and deemed the index lesion—and one or more separate, secondary tumour foci of smaller volume. Much laboratory and clinical evidence has shown that we need to rethink how we regard low-grade and low-volume prostate lesions. In this Personal View, we discuss why small, low-grade Gleason pattern prostate lesions, which are currently designated as prostate cancer, could be regarded as non-malignant. These lesions either do not meet the criteria of the hallmarks of cancer or robust evidence that they do so is absent, by contrast with large lesions with a high Gleason grade, which seem to cause most metastatic disease.





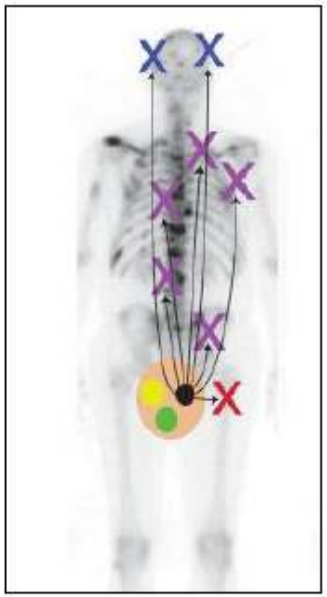
The index lesion is define as the largest volume lesion
This lesion is presumed to be the main driving factor for the overall behavior and lethality of the cancer

Lancet Oncology Nov 2012

Copy number analysis indicates monoclonal origin of lethal metastatic prostate cancer

Wennuan Liu[1,9], Sari Laitinen[2,9], Sofia Khan[3], Mauno Vihinen[3], Jeanne Kowalski[4], Guoqiang Yu[5], Li Chen[5], Charles M Ewing[6], Mario A Eisenberger[7], Michael A Carducci[7], William G Nelson[7], Srinivasan Yegnasubramanian[7], Jun Luo[6,7], Yue Wang[5], Jianfeng Xu[1], William B Isaacs[6,7], Tapio Visakorpi[2] & G Steven Bova[6–8]

- ✓ Isolated DNA from 94 anatomically separate cancer sites in 30 men who died from M+ PCa
- ✓ High-resolution genome-wide single nucleotide polymorphism and copy number survey: Metastatic PCa have clonal origins in most, if not all cases
- ✓ In other words, metastatic deposits taken from men in a rapid autopsy protocol shared one common cell of origin deriving from a single genomically aberrant cell

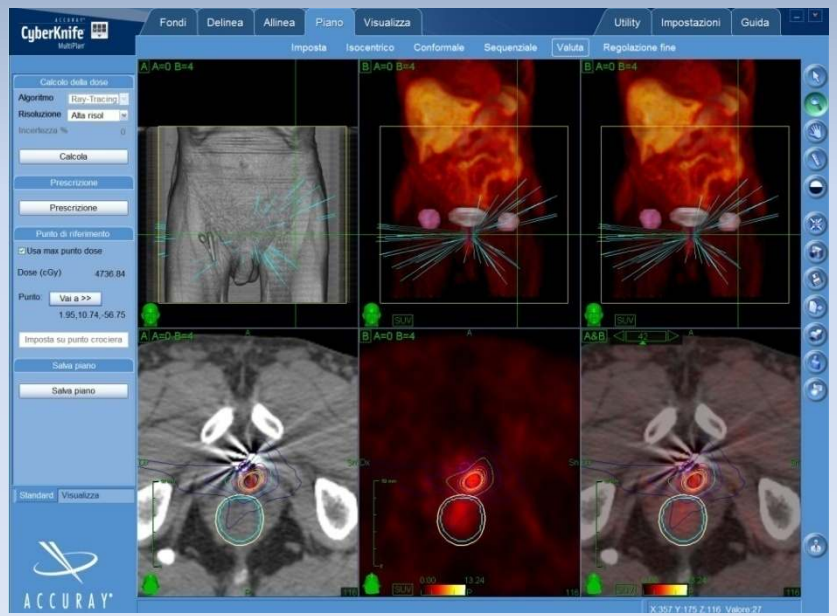


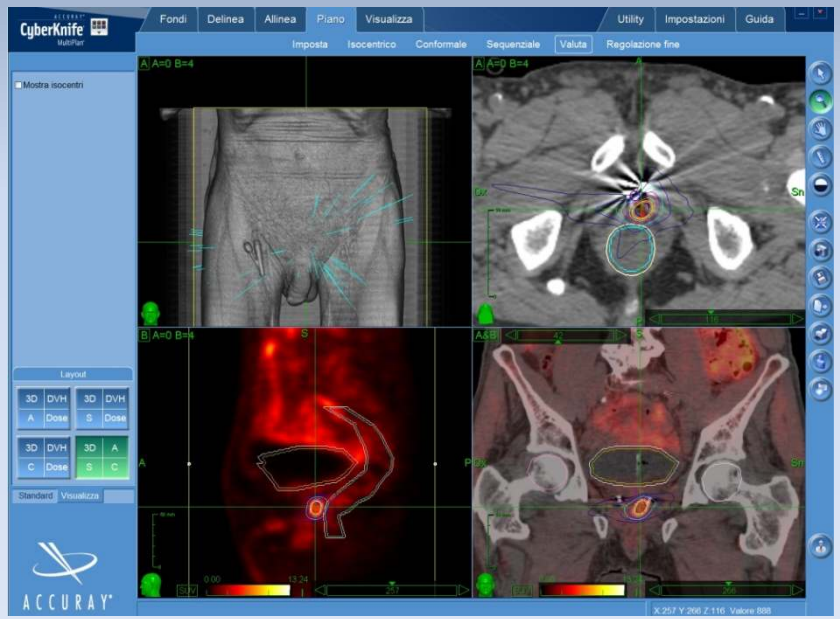
Nature Medicine 2009

Image – guided Robotic Radiosurgery treatment as salvage therapy for locally recurrent prostate cancer following EBRT

December 2012 - June 2014 : 14 patients

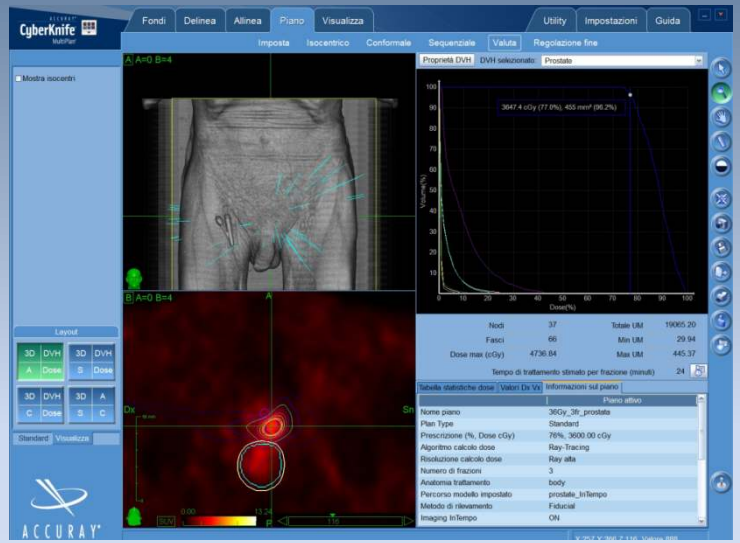
Image guided facilitates targetting





Positron Emission Tomography (PET) and CT scan Images were fused for target volume delineation

Image – guided Robotic Radiosurgery treatment as salvage therapy for locally recurrent prostate cancer following EBRT



Treatment regimen consisted of 3 fractions of 10-12 Gy
for a total dose of 30-36 Gy

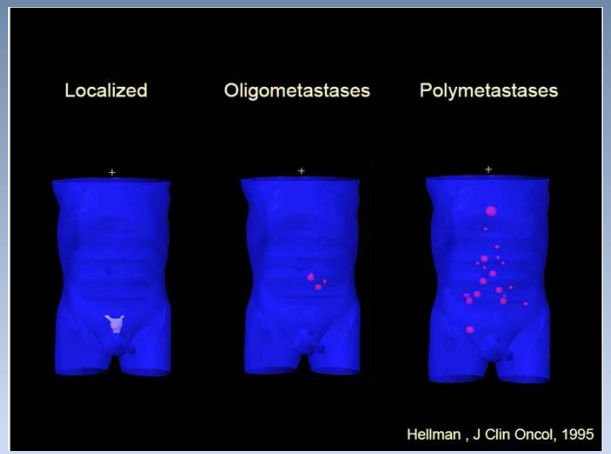
The Cyberknife treatment was well tolerated without any rtog grade 3 acute or late toxicity. With a median follow up of 11 months (range 3-22) we observed the following results: no in field recurrence, resulting in a local control of 100%. In 3 patients, respectively at 11, 13 at 21 months we recorded biochemical recurrence with a new CT/PET positive prostate node outside the irradiated field requiring a second Cyberknife salvage treatment.

No metastatic disease

Robotic image – guided Stereotactic Radiotherapy for isolated Lymph node

Table 5 SBRT of abdominal lymph node oligometastases

	Patients (N)	Primary cancer	Dose (Gy) × fr	Median follow up (mos)	Outcomes
Jereczek-Fossa et al. 2009 [53]	14	Prostate	33 (mean) × 3-5	Mean 18.6	- No in-field clinical progression - Distant or regional LN progression at mean time of 12.7 mo - All patients with relapse had high-risk disease
Bignardi et al. 2011 [54]	19	CRC (5/19)	45 × 6	12	Actuarial rate of freedom from local progression: 77.8 ± 13.9 at both 12 and 24 mos Minimal acute and chronic toxicity
Choi et al. 2010 [55]	30	Uterus and cervix	EBRT: 27–45 (n = 4 pts) SBRT: 33–45 × 3 (n = 24 pts)	15	4-year LC rate: 67.4% 4-year OS rate: 50.1% (all 30 pts).
Kim et al. 2009 [56]	7	Gastric (salvage aftersurgery)	48 (median) × 3	26	Complete response: n = 5 Partial response: n = 2
Kim et al. 2009 [57]	7	CRC	Escalated dose 36–51 × 3	26	Median survival: 37 mos 1-year OS: 100% 3-year OS: 71.4% G4: intestinal obstruction in 1/7 patients
Bae et al. 2012 [51]	41	CRC	48(45 – 60) × 3	28	-PFS, LC and OS rates 3-year rates : 40%, 64%, 60% 5-year rates : 40, 57%, 38% -G3 perforation after pelvic LN SBRT;G4 obstruction of para-aortic LN SBRT



Hellman and Weichselbaum (1995).. *"there is a subgroup of patients with an intermediate phase of metastatic disease, that presents a potential for disease control with the ablation of the few metastases"*

Robotic stereotactic radiotherapy

Linac-based or robotic image-guided stereotactic radiotherapy for isolated lymph node recurrent prostate cancer

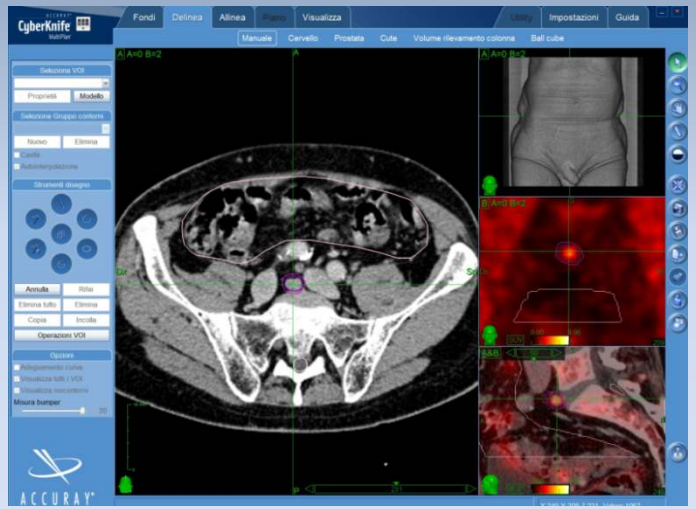
Barbara A. Jereczek-Fossa [a,g,*], Laura Fariselli [e,f], Giancarlo Beltramo [e], Gianpiero Catalano [a], Flavia Serafini [a], Cristina Garibaldi [b], Raffaella Cambria [b], Lorenzo Brait [e], Marco Possanzini [e], Livia C. Bianchi [e], Andrea Vavassori [a], Dario Zerini [a], Franco Orsi [d], Ottavio de Cobelli [c,g], Roberto Orecchia [a,g]

Radiotherapy and Oncology. 2009

Robotic image – guided Stereotactic Radiotherapy for isolated Lymph node

March 2009 – March 2013 : 30 patients, 47 lesions

Median follow up: 33 months (range 13 -73)

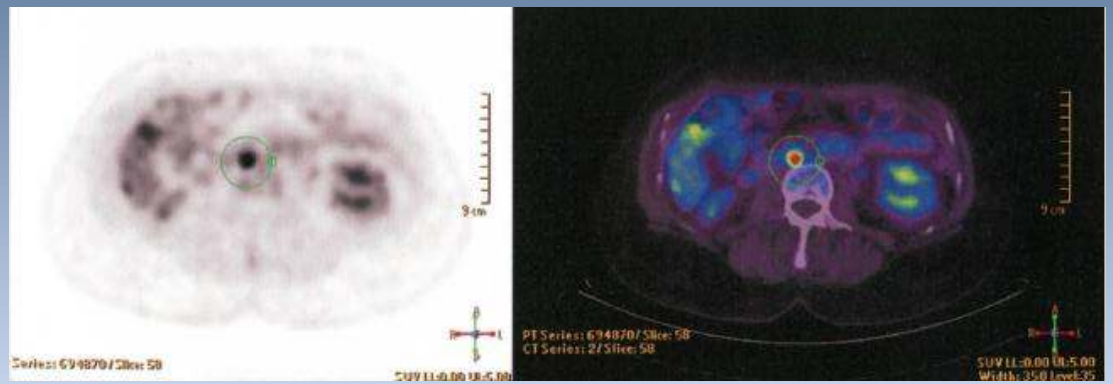


TC-PET image Fusion

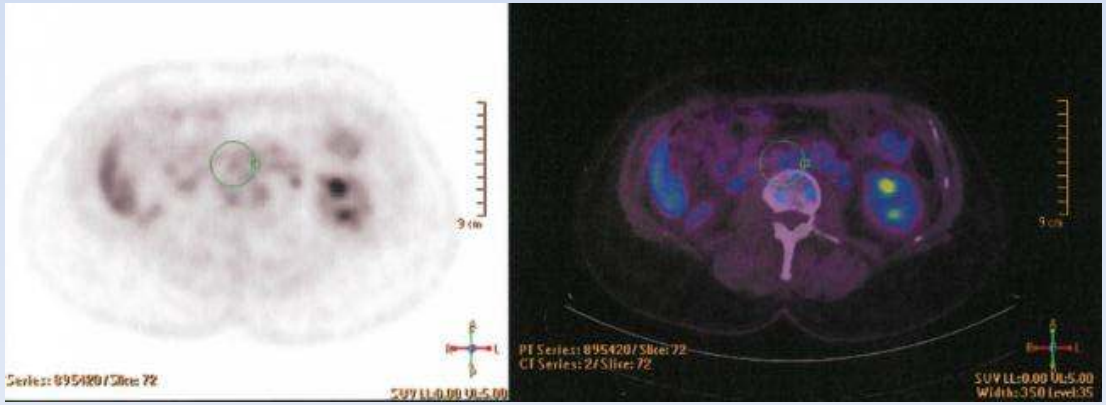
Treatment regimen consisted of 3 fractions of 10-12 Gy for a total dose of 30-36 Gy

The Cyberknife treatment was well tolerated without any acute or late toxicity at all. There were no in field recurrence, resulting in a local control of 100%. Eleven and 3 patients, respectively required a second and third salvage treatment for metacronous metastatic disease. The median time to clinical progression was 14 months (range 3-54).

Results



Before CK SBRT Treatment



After CK SBRT Treatment

B.A. Jereczek-Fossa[1,6] · I. Bossi-Zanetti[1,6] · R. Mauro[1,6] · G. Beltramo[3] · L. Fariselli[4] · L.C. Bianchi[3] · C. Fodor[1] · P. Fossati[1,2,6] · G. Baroni[2,5] · R. Orecchia[1,2,6]

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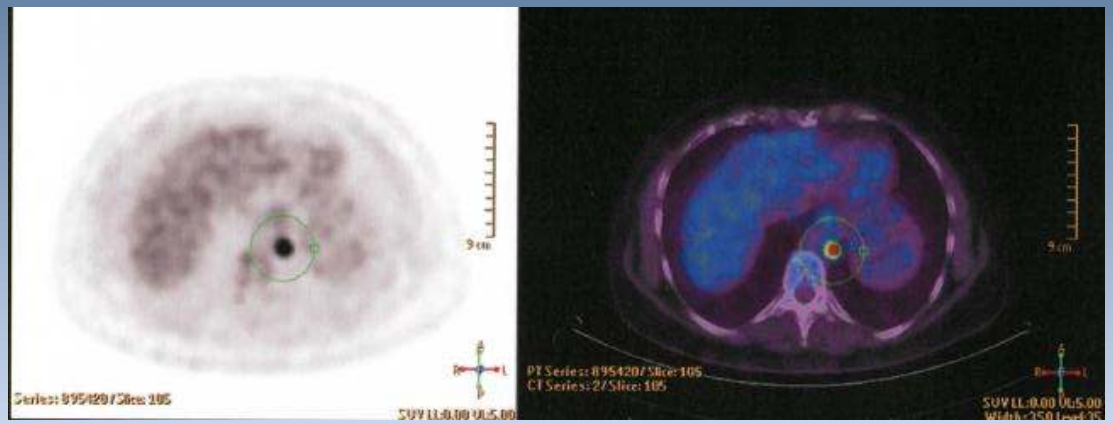
[5] Department of Bioengineering, Politecnico di Milano, Milan
[6] University of Milan

CyberKnife robotic image-guided stereotactic radiotherapy for oligometastic cancer

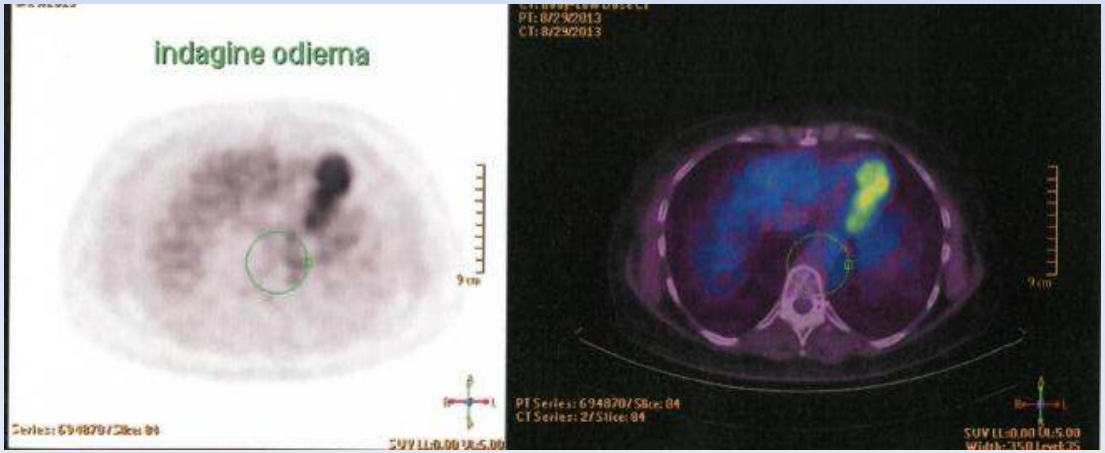
A prospective evaluation of 95 patients/118 lesions

Strahlenther Onkol 2013, 189: 448-455

Results



Before CK SBRT Treatment



After CK SBRT Treatment

B.A. Jereczek-Fossa[1,6] · I. Bossi-Zanetti[1,6] · R. Mauro[1,6] · G. Beltramo[3] · L. Fariselli[4] · L.C. Bianchi[3] · C. Fodor[1] · P. Fossati[1,2,6] · G. Baroni[2,5] · R. Orecchia[1,2,6]

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CyberKnife robotic image-guided stereotactic radiotherapy for oligometastic cancer

A prospective evaluation of 95 patients/118 lesions

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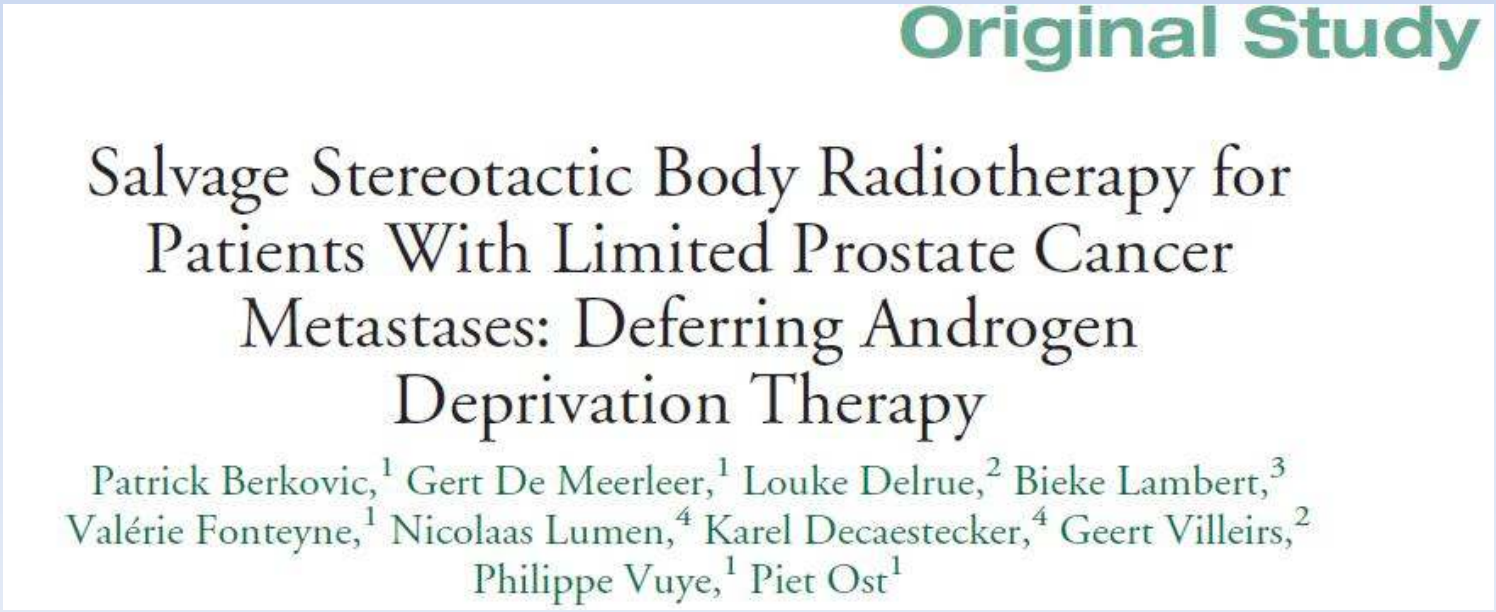
Take home message

- Cyberknife SBRT is a feasible approach or isolated recurrent lymph node with excellent in-field tumor control and low toxicity profile

- It is also important to bear in mind that effective local therapy might reduce the burden of the systemic therapies usually given to these categories of patients with longer survival and excellent quality of life


Original Study

Salvage Stereotactic Body Radiotherapy for Patients With Limited Prostate Cancer Metastases: Deferring Androgen Deprivation Therapy

Patrick Berkovic,[1] Gert De Meerleer,[1] Louke Delrue,[2] Bieke Lambert,[3] Valérie Fonteyne,[1] Nicolaas Lumen,[4] Karel Decaestecker,[4] Geert Villeirs,[2] Philippe Vuye,[1] Piet Ost[1]

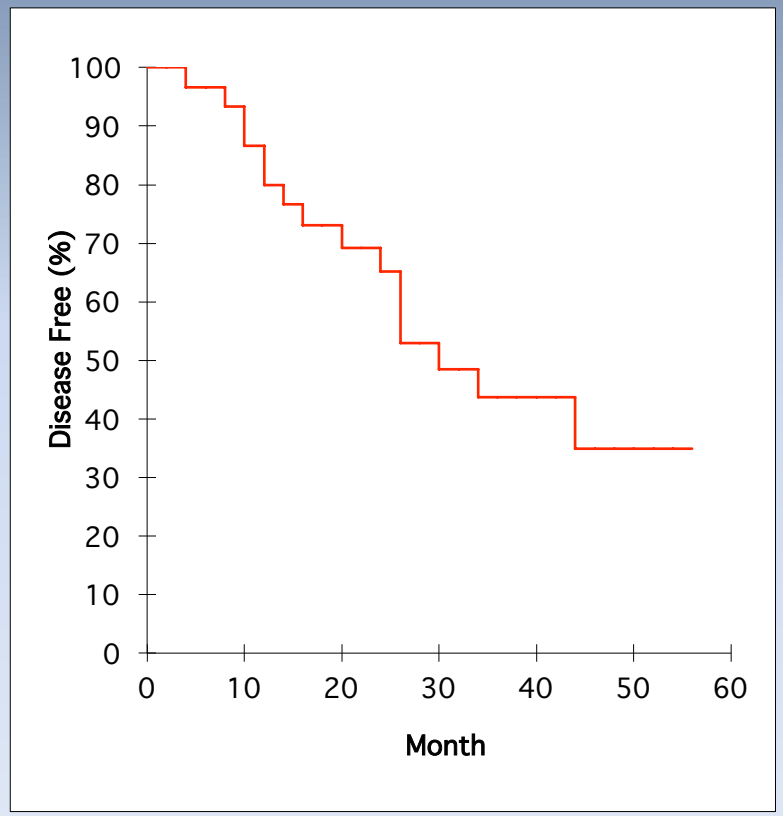
Clinical Genitourinary Cancer march 2013

Salvage stereotactic body for patients with limited prostate cancer metastases: deferring ADT

The median time to clinical progression was 14 months (range 3-54).

After a median follow up of 33 months (range 13-73), 16 patients started with ADT because of polymetastatic disease resulting in an ADT-FS of 80% at 1 year and 65% at 2 years.

The median time Androgen deprivation therapy (ADT) was deferred resulted of 26 months (range 4-56).



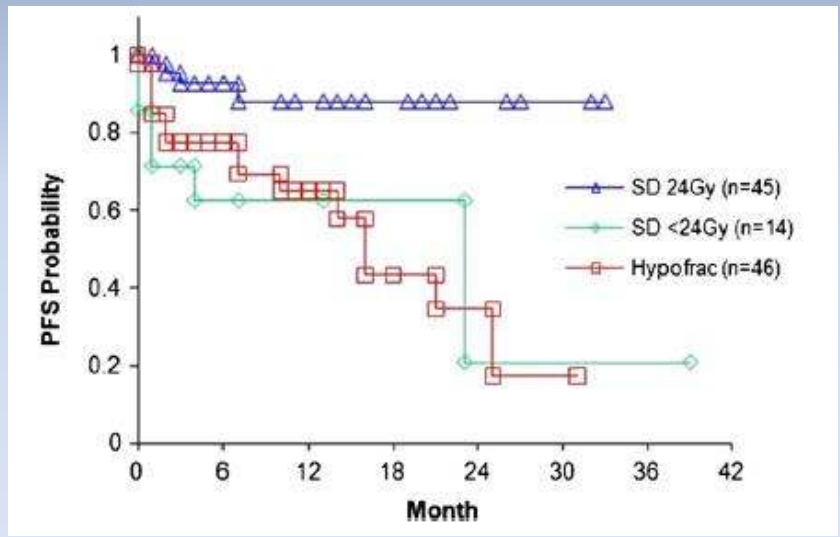
SBRT in bone oligometastasis

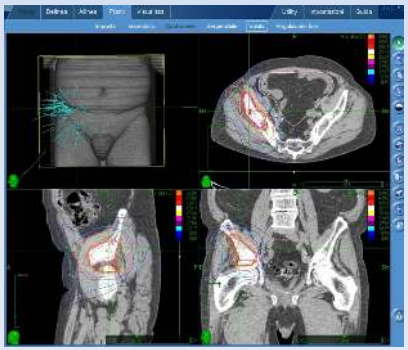
CLINICAL INVESTIGATION **Metastases**

TUMOR CONTROL OUTCOMES AFTER HYPOFRACTIONATED AND SINGLE-DOSE STEREOTACTIC IMAGE-GUIDED INTENSITY-MODULATED RADIOTHERAPY FOR EXTRACRANIAL METASTASES FROM RENAL CELL CARCINOMA

Michael J. Zelefsky, M.D.,* Carlo Greco, M.D.,* Robert Motzer, M.D.,‡
Juan Martin Magsanoc, M.D.,* Xin Pei, Ph.D.,* Michael Lovelock, Ph.D.,†
Jim Mechalakos, Ph.D.,† Joan Zatcky, N.P., R.N.,* Zvi Fuks, M.D.,* and Yoshiya Yamada, M.D.*

The 3 year local progression free survival for the group who received a high single-dose (24 Gy n=45 pts) was 88% vs 21% and 17% respectively

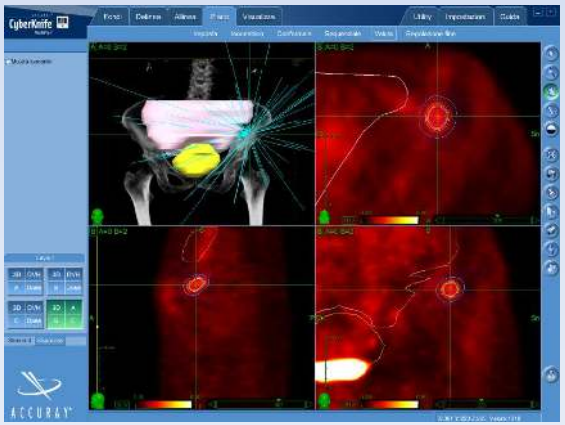


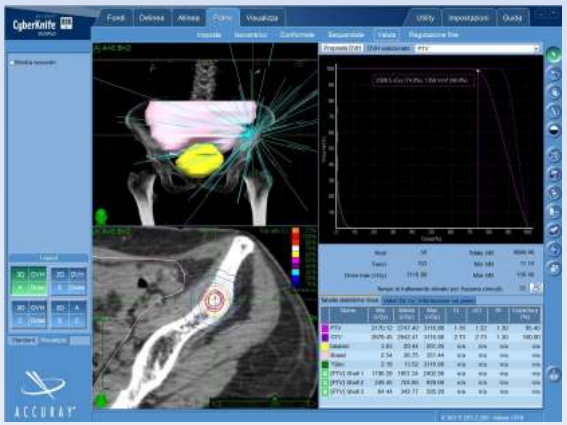


Actuarial local control as a function of prescription regimen

SBRT in bone oligometastasis

Author	Pts/Lesions	Fractionation	Tumour size	Follow-Up	Loca control	OS	Toxicity
Ryu S et Al. 2004	49 / 61 spinal lesionsi	10-16 Gy Single fraction	single vertebral body	6-24 mos	Pain control 85% patientsi	/	/
Yamada Y et Al. 2007	93 / 103 Spinal	18-24 Gy Single fraction	44-316 cm3	15 mos (2-45)	LC 90% Pain control in 100% with dose of 21Gy	OS 15 mos	1 G3 pain 2 vertebral fracture 2 esophagitis G2 1 tracheo-esofageal fistula
Milano MT et Al. 2008	121 / 293 22 bone	50 Gy/5Fr	21.5 ml (0.03-422.4)	41 mos (27-77)	LC 2yrs 67% LC 4yes 60% PFS 2yrs 26% PFS 4yrs 20%	OS 50% OS 28%	1 pleural effusion
Greco C et Al. 2010	103 / 126 94 bone	18-24 Gy Single fraction	104.8 cm3 (8.5-1150)	18 mos (2-45)	LC 2yrs 85% (23/24 Gy) LC 2yrs 38% (21/22 Gy) LC 2yrs 25% (18/20 Gy)	/	ACUTE: 2 Gatrointestinal G3 LATE (G3<4%): 1 Gatrointestinal G3 3 radicolopathy 3 peripheral neuropatihy
Nguyen QN et Al. 2009	48 / 55 spinal	24 Gy single Fr (8) 27 Gy/3Fr (34) 30 Gy/5Fr (13)	24-210 cm3	13.1 mos (3.3-54.5)	LC 1aa 82.1% Pain controllo 64% at 9 mos	OS 1yr 2% Median survival 22 mos	pain G3 2% Anemia G3 2% Fatigue G2 13% Nausea G2 11% Sickness G2 7%





EUROPEAN UROLOGY 59 (2011) 572–583

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European Association of Urology

Guidelines

EAU Guidelines on Prostate Cancer. Part II: Treatment of Advanced, Relapsing, and Castration-Resistant Prostate Cancer

	Isotope	N. Of Pts	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
Picchio et al	11C	100	46	-	-	-
De Jong et al	11C	36	38	-	-	-
Cimitian et al	18F	100	98	100	-	-
Rinnab et al	11C	50	95	40	86	67
Scattoni et al	11C	25	64	90	86	72
Reske et al	11C	49	73	88	92	61
Krause et al	11C	63	56	-	-	-
Castellucci et al	11C				-	-
Breeuwsma et al	11C			00	100	44
Giovacchini et al	11C			3	91	87
Husarik et al	18F				-	-
Pelosi et al	18F	56	43	-	-	-

SENSITIVITY: 39-98%
SPECIFICITY: 40-100%
PPV: 86-100%
NPV: 44-87%

ASSESMENT	INDICATIONS
PSA and DRE	- PSA should be the only diagnostic test until documented BCR - DRE can be helpful in detecting local relapse
TRUS + biopsy	Not recommended
CT scan	Used to detect distant metastases
MRI	Not routinely recommended (preliminary studies show that it is more sensitive than bone scan in detecting bone lesions)
Bone scan	PSA>20 ng/mL, or PSA>10 ng/mL and PSADT< 6mo
PET/CT	Not routinely recommended (promising in detecting local, nodal and bone recurrences)

Guidelines recommendations on when to perform imaging studies in case of BCR after primiry treatment

Take home message

	PERFORMANCE CHARACTERISTICS^	
	After RP	After RT
Local recurrence*	Poor	Good (?)
Nodal recurrence	Good	Good
Bone metastases	Promising (few data) High sensitivity and specificity	Promising (few data) High sensitivity and specificity

- PET/CT represents a new tool in the armamentarium of oncologist for assesment of cancer recurrence
- It show good accuracy in detecting nodal and bone recurrence after primary local treatment
- Low accuracy in detecting local recurrence after RP better after EBRT
- Main limitations: spatial resolution (potentially missing micrometastatic disease < 5 mm)
- Choline PET/CT showed to significantly impact on patient management and might contribute to a non-individualized systemic therapy to a lesion-targeted approach, thus potentially reducing use and side effects of ADT