Metastasi linfonodali

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Società Italiana di Radiobiologia

XXIX Congresso Nazionale AIRB

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Firenze 13-14 Giugno 2014

IEO Arc Advanced Radiotherapy Center

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EXPERT REVIEWS

New concepts and insights into the role of radiati
therapy in extrac

The Role of Ster
in the Tre

Experiences from 2009-2014

body Radiotherapy
ients With Single Abdominal
Node Recurrent Cancer

Ba. k-Fossa, MD, PhD,*† Gaia Piperno, MD,* Sara Ronchi, MD,*† Gianpiero Catalano, MD,‡

Stereotactic body radiotherapy for oligometastases

Alison C Tree, Vincent S Khoo, Rosalind A Eeles, Merina Ahmed, David P Dearnaley, Maria A Hawkins, Robert A Huddart, Christopher M Nutting, Peter J Ostler, Nicholas J van As

Oligometastatic patients

The clinical state of oligometastatic disease was proposed in 1995 by Hellman and Weichselbaum.

They hypothesized that, in some patients with a limited number of clinically detectable metastatic tumors, the extent of disease exists in a transitional state between localized and widespread systemic disease.

In this model, oligometastatic disease has the potential of progressing to widespread metastatic disease.

Local control (LC) of oligometastases may yield improved systemic control

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Lymph-node recurrence from…

stereotactic body radiotherapy (SBRT)

The fundamental principles include:

The delivery of very high doses of radiation in each treatment session (or “per fraction”).

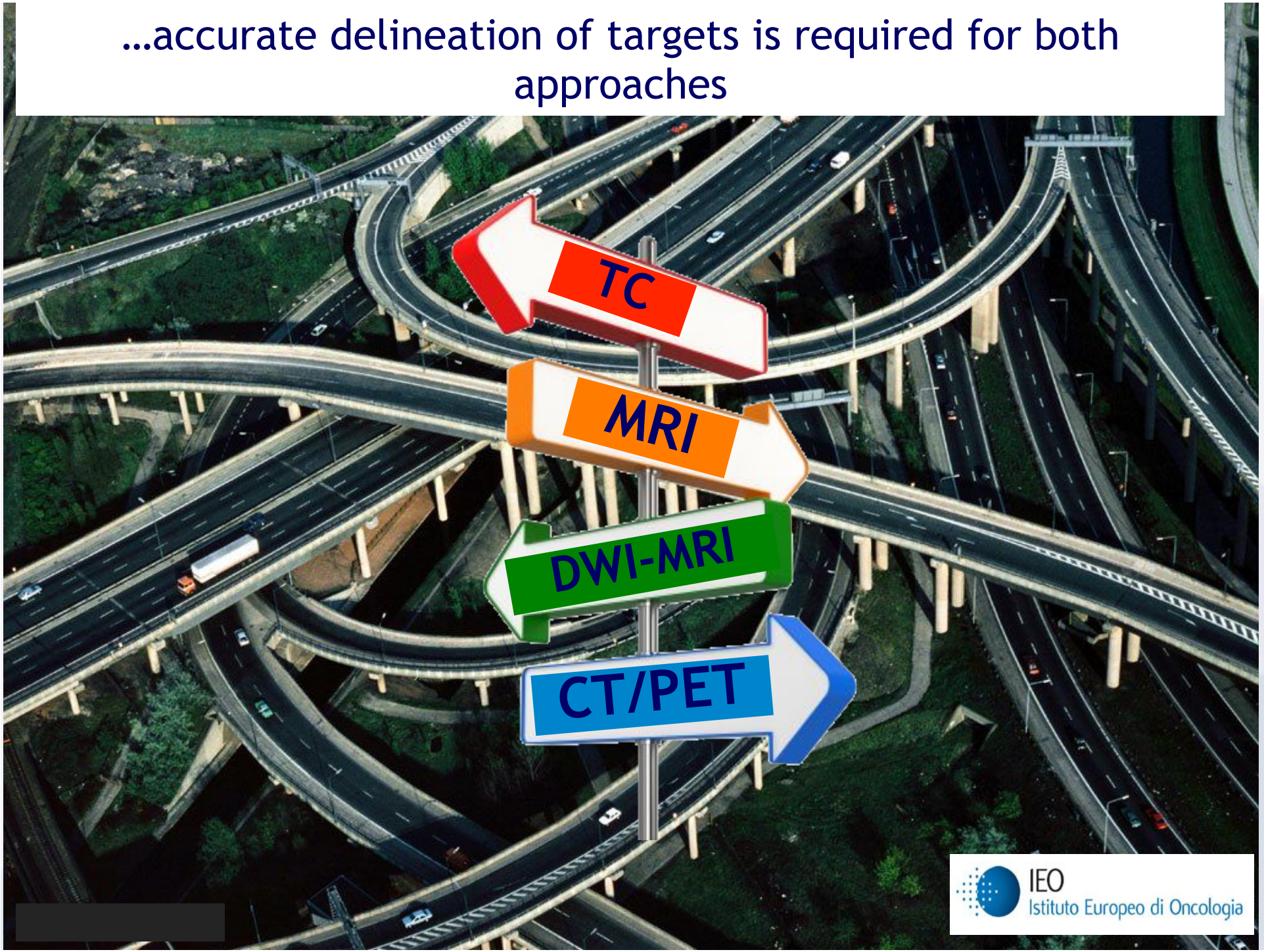
The dose delivered rapidly must dissipate or “drop off “steeply in the surrounding normal tissues in order to minimize their exposure to excessive doses

The total dose to be delivered is given over a short overall time interval, i.e., over a few sessions (short fractionation).

There are tumor size and number of nodes limitations; i.e., SBRT is preferentially used only for small (e.g., smaller than 5 cm) discrete targets .

Curr Oncol Rep (2014) 16:391

…accurate delineation of targets is required for both approaches



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EXPERT REVIEWS

New concepts and insights into the role of radiation therapy in extracranial metastatic disease

Expert Rev. Anticancer Ther. 13(10), 1145–1155 (2013)

Umberto Ricardi[1], Andrea Riccardo Filippi*[1] and Pierfrancesco Franco[2]

Table 4. Selected studies on stereotactic ablative radiotherapy in lymph nodes metastases.

Study (year)	Patients (n)	Primary tumor	Treated sites	Dose and fractionation	Median follow-up (months)	Local control	Overall survival	Toxicity
Choi *et al.* (2009)	30	Miscellaneous	Abdominal nodes	33–45 Gy/3 fractions	15	4 years: 67.4%	4 years: 50.1%	Late G3: 5%
Jereczek-Fossa *et al.* (2009)	14	Prostate	Pelvic nodes	30 Gy/3 fractions	18.6	Crude: 100%	Not reported	Late G2: 7%
Kim *et al.* (2009)	7	Stomach	Para-aortic nodes	48 Gy/3 fractions	26	Crude: 100%	3 years: 43%	G3/G4: 0%
Kim *et al.* (2009)	23	Rectum	Pelvic nodes	39 Gy/3 fractions	26	Crude: 86%	3 years: 71.4%	Late G4: 14%
Casamassima *et al.* (2011)	25	Prostate	Pelvic/para-aortic/ mediastinal nodes	30 Gy/10 fractions	29	3 years: 90%	3 years: 92%	>G2: 0%
Bignardi *et al.* (2011)	19	Miscellaneous	Abdominal nodes	45 Gy/6 fractions	12	1 year: 77.8%	2 year: 93.3%	G3: 5%

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Other last experience…

Bonomo et al. 2013	**26 pts, 32 abdomino-pelvic LN mts**	**retrospective**	**LINAC with dynamic arcs and CBK**	**miscellaneous (most common: gynecologic, and prostate)**
Alongi et al. 2012	25 pts, 28 abdomino-pelvic LN mts	retrospective	VMAT RapidArc using FFF beams	miscellaneous
Corvò et al. 2012	36 pts, 36 abdomino-pelvic LN mts	retrospective	IG-IMRT (helical Tomotherapy ™ Hi-ART)	miscellaneous, (most common pancreas and colon)

LC rate 80-90%

Mean follow-up < 2 years

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Linac-based Stereotactic Body Radiotherapy for Oligometastatic Patients With Single Abdominal Lymph Node Recurrent Cancer

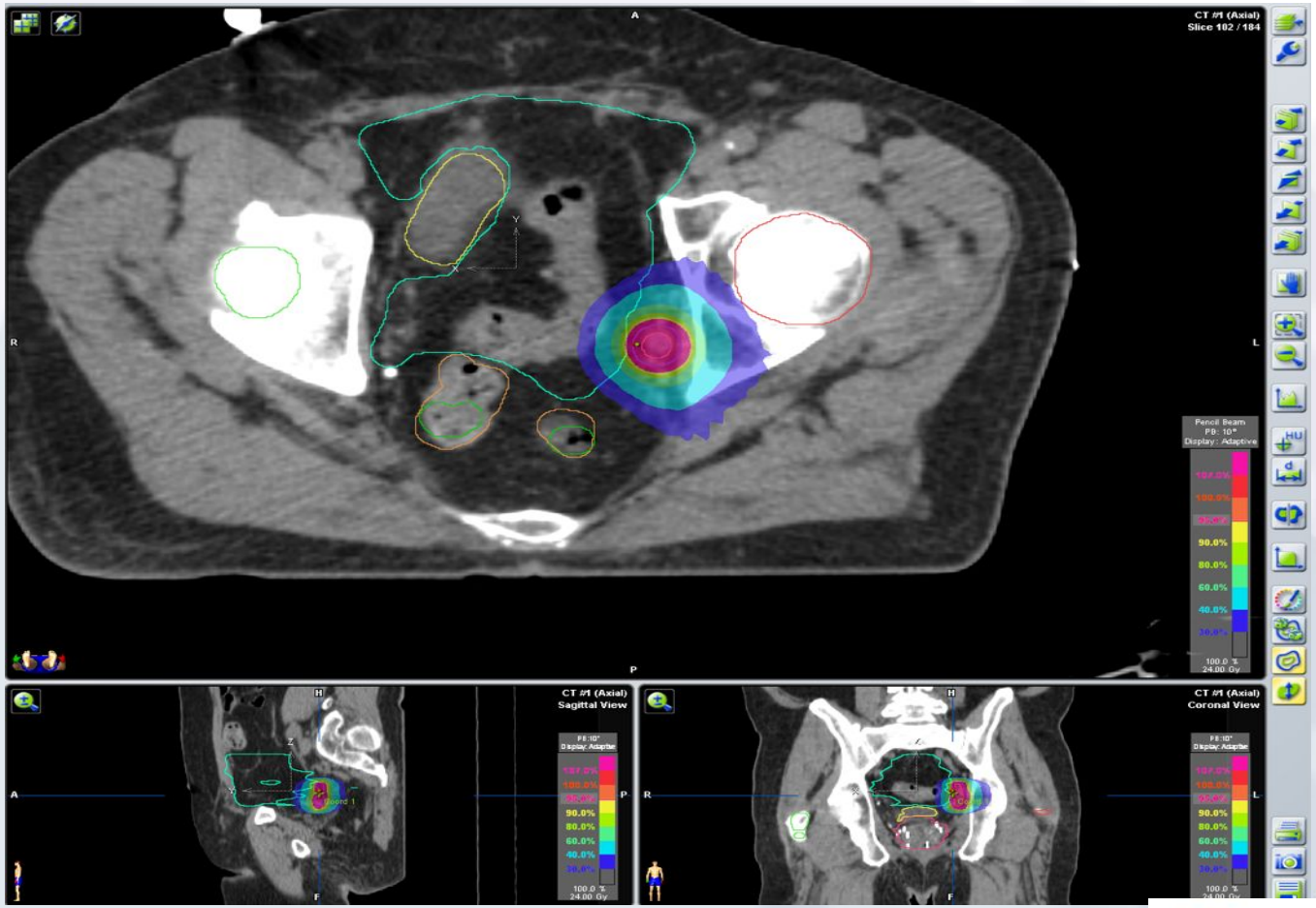
Barbara A. Jereczek-Fossa, MD, PhD,† Gaia Piperno, MD,* Sara Ronchi, MD,*† Gianpiero Catalano, MD,‡ Cristiana Fodor, MSc,* Raffaella Cambria, MSc,§ Piero Fossati Ing, MD,*†‖ Federica Gherardi, MD,* Daniela Alterio, MD,* Dario Zerini, MD,* Cristina Garibaldi, MSc,§ Guido Baroni, PhD,‖¶ Ottavio De Cobelli, MD,†# and Roberto Orecchia, MD*†‖*

TABLE 2. Treatment Outcome (N = 69 Patients, n = 94 Lesions, ie, Abdominal Lymph Nodes)

Outcome	LN	M	Total
Acute toxicity of SBRT (for all lesions, n = 94)			
Yes*	7	25	32 (34.0%)
No	23	39	62 (66.0%)
Late toxicity of SBRT (for 69 patients)			
Yes†			8 (11.6%)
No			51 (73.9%)
Non evaluable			10 (14.5%)
Follow-up duration (mo)			
Median (range)			20 (1–92)
Response to SBRT (all lesions, n = 94)			
Radiologic and/or FDG-or-choline-PET/CT response			
Evaluable	25 (26.6%)	56 (59.6%)	81 (86.2%)
Complete response	11	25	36 (44.0%)
Partial response	8	13	21 (26.0%)
Stable disease	6	14	20 (25.0%)
Progression	0	4	4 (5.0%)
Nonevaluable	5 (5.3%)	8 (8.5%)	13 (13.8%)
Radiologic response to SBRT in the lesions treated with SBRT only, with no concomitant systemic therapy (n = 59, 52 evaluable)			
Complete response	7	15	22 (42.0%)
Partial response	5	9	14 (27.0%)
Stable disease	4	10	14 (2.0%)
Progression	0	2	2 (4.0%)
Non evaluable	2	5	7 (12.0%)
Disease progression			49 patients (87 progressions)
Site of primary progression (49 patients)			
Only in SBRT field			1
Out of SBRT field			35‡
Only biochemical			5
In SBRT field + out of SBRT field			8
Site of progression (at any time) (87 progressions)			
In SBRT field			6
Out of SBRT field			58§
Biochemical			7
In SBRT field + out of SBRT field			16‖

SBRT options

SBRT with VERO



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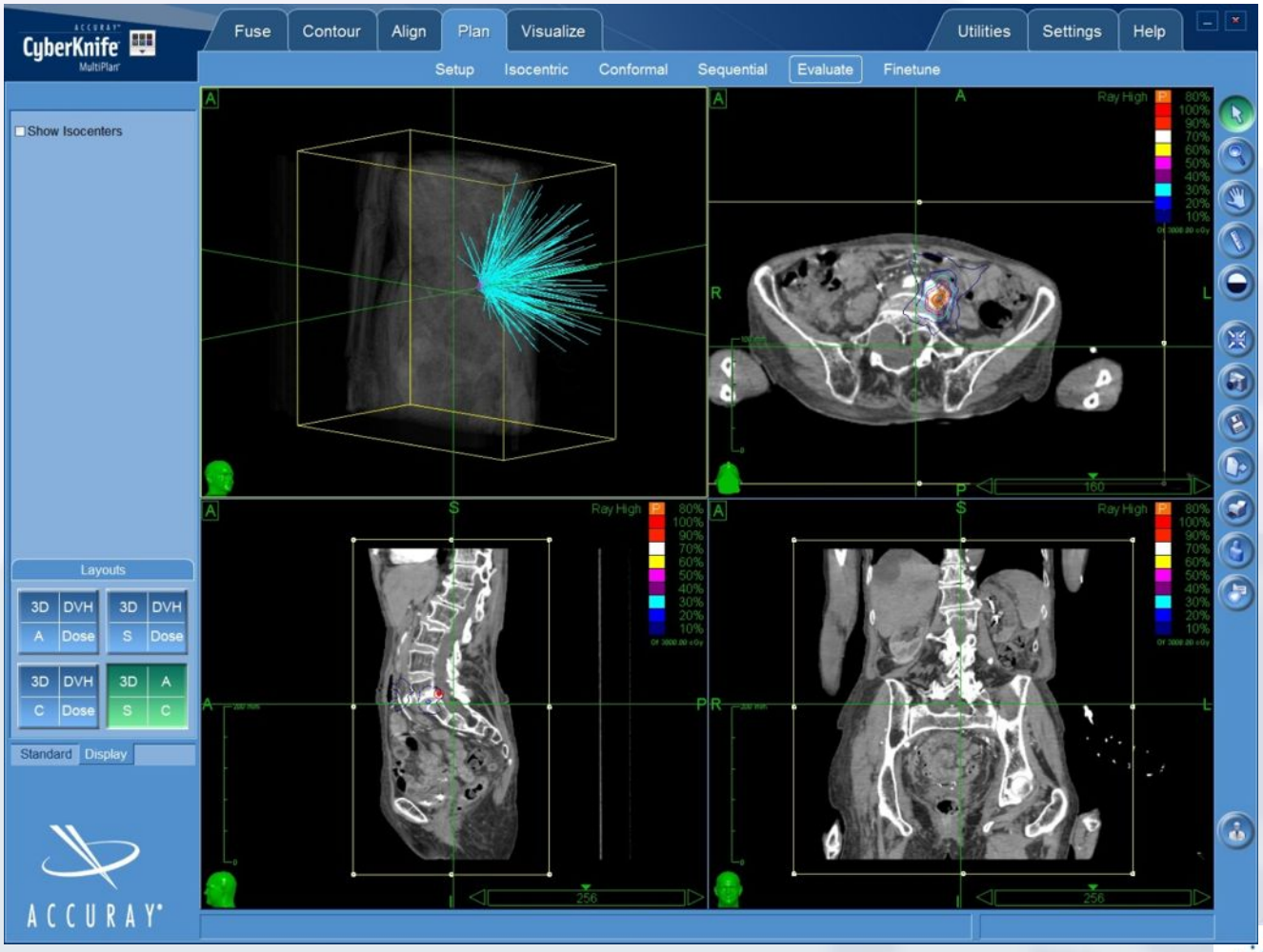
SBRT with Cyberknife



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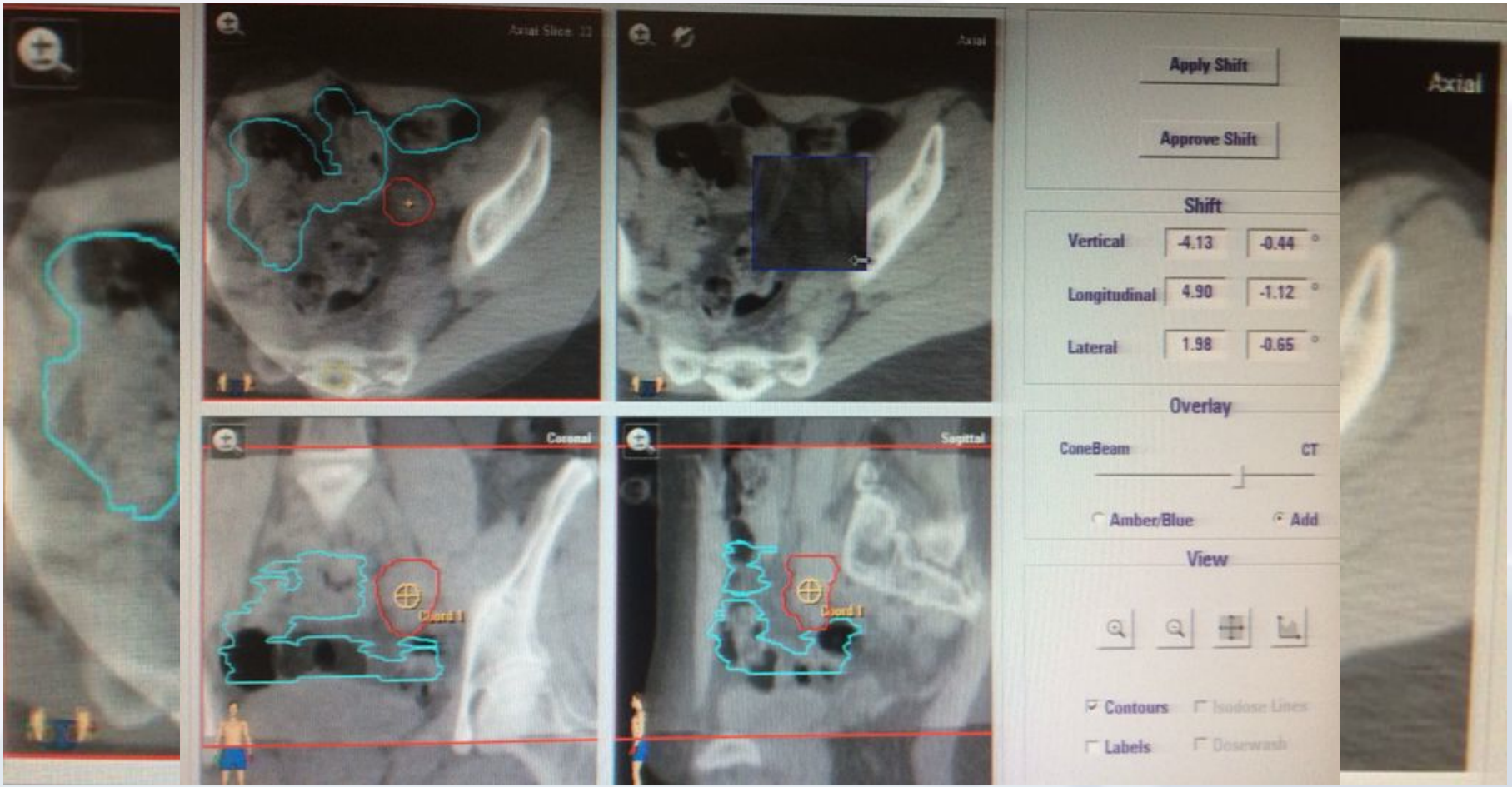
SBRT with VERO: IGRT-CBCT



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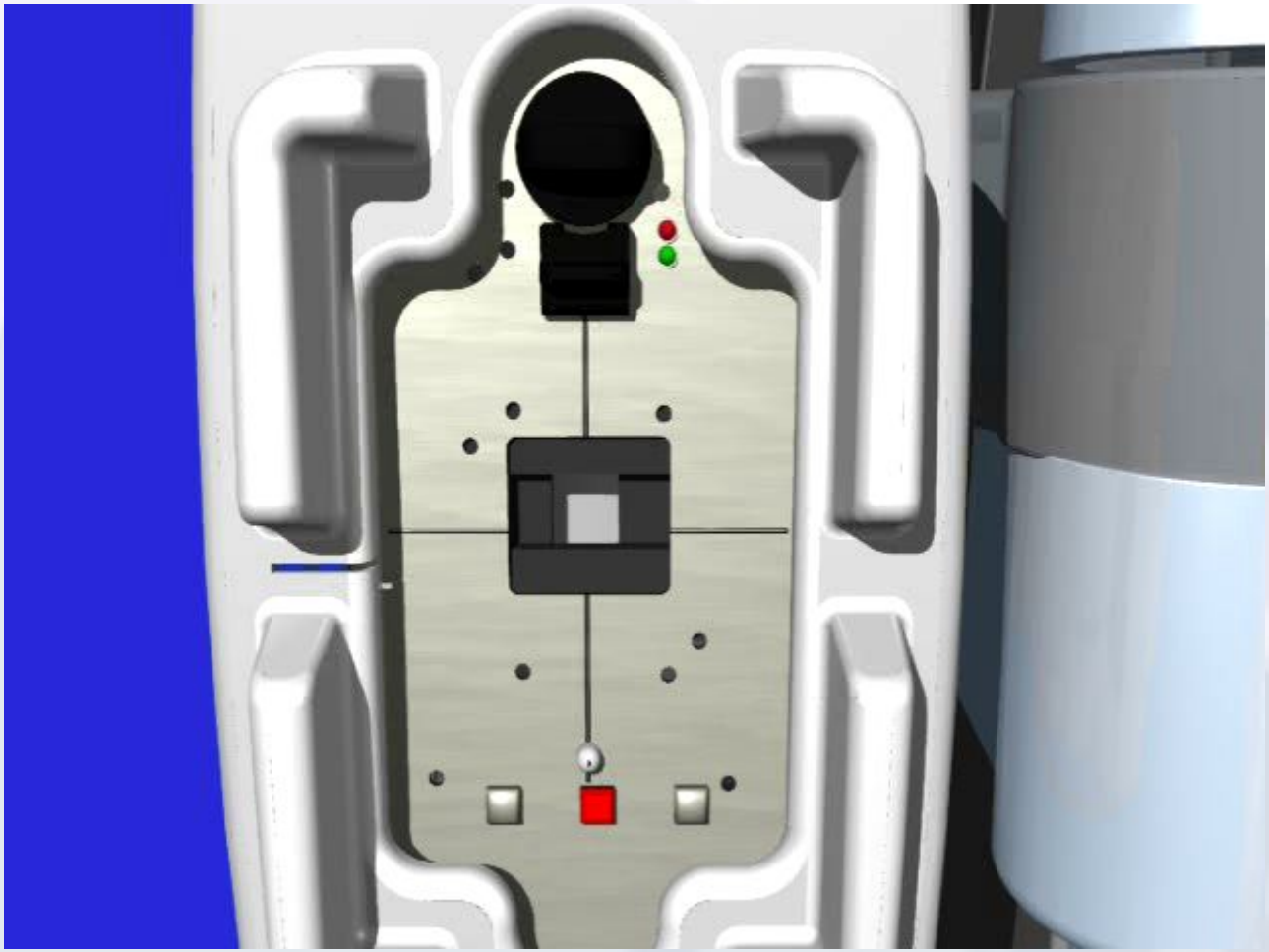

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SBRT **UNLEASHED**

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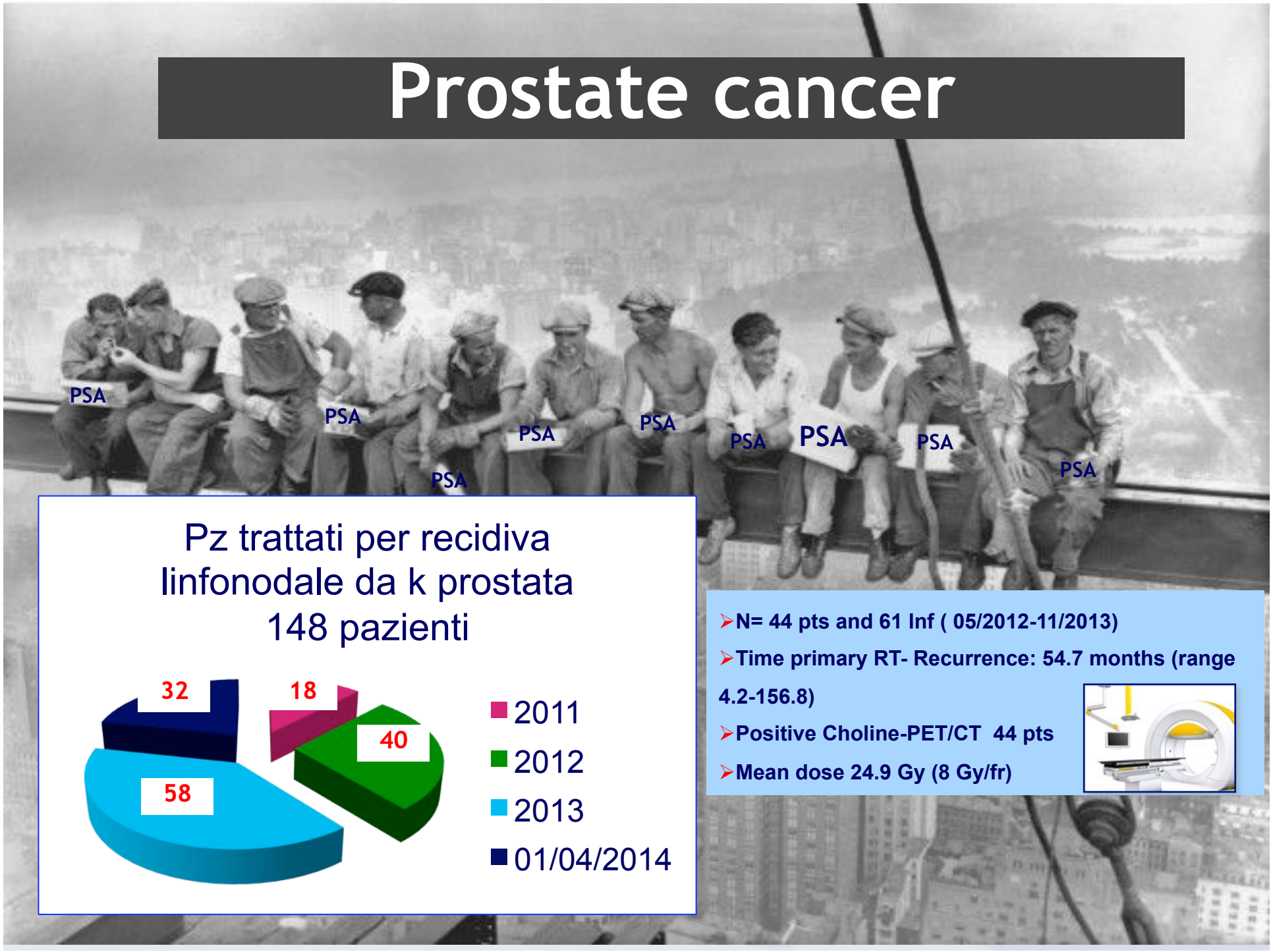
Prostate cancer



Pz trattati per recidiva linfonodale da k prostata 148 pazienti

- N= 44 pts and 61 Inf (05/2012-11/2013)
- Time primary RT- Recurrence: 54.7 months (range 4.2-156.8)
- Positive Choline-PET/CT 44 pts
- Mean dose 24.9 Gy (8 Gy/fr)

Pz 1

Anamnesi oncologica:

24.07.09 Prostatectomia radicale + LAD. EI: pT3a pN0(0/39) M0 Gleason (4+3) a Roma
09.2009 PSA 0.1
10.2009 PSA 0.2
12.2009 - 2.2010 RT adj sec. IMRT (70 Gy sulla loggia c/o Regina Elena, Roma) , tp farmacologica con bicalutamide x 1 anno
2.2013 PSA 0.25
3.2013 PSA 0.37
4.2013 PSA 0.47
5.2013 PSA 0.41
30/6/2013 PSA 0.12
13.5.13 RM della loggia prostatica: in sede perianastomotica posteriore paramediana sx ispessimento tissutale nodulariforme di 9 x 6 mm (sospetta recidiva), localizzato a circa 18 mm dallo sbocco ureterale

08/2013 biopsia dell'anastomosi in IEO:negativa

PSA 10/2013 0.27
PSA 11/20130.40
PSA 22/02/2014 0.54
PSA 03/2014 1.1

RM 25/11/2013:esame confrontato con quello del 13/5/13 stabile l' ispessimento tiissutale stabile per morfologia e dimensioni(9x6 mm)

RM 28/03/2014: nodulo di 5 mm a livello del collo vescicale sul versante postero laterale subito sopra la giunzione vescico-ureterale compatibile con recidiva.

04/2014 PET colina: positiva per nodulo di 1 cm in prossimità dell'anastomosi

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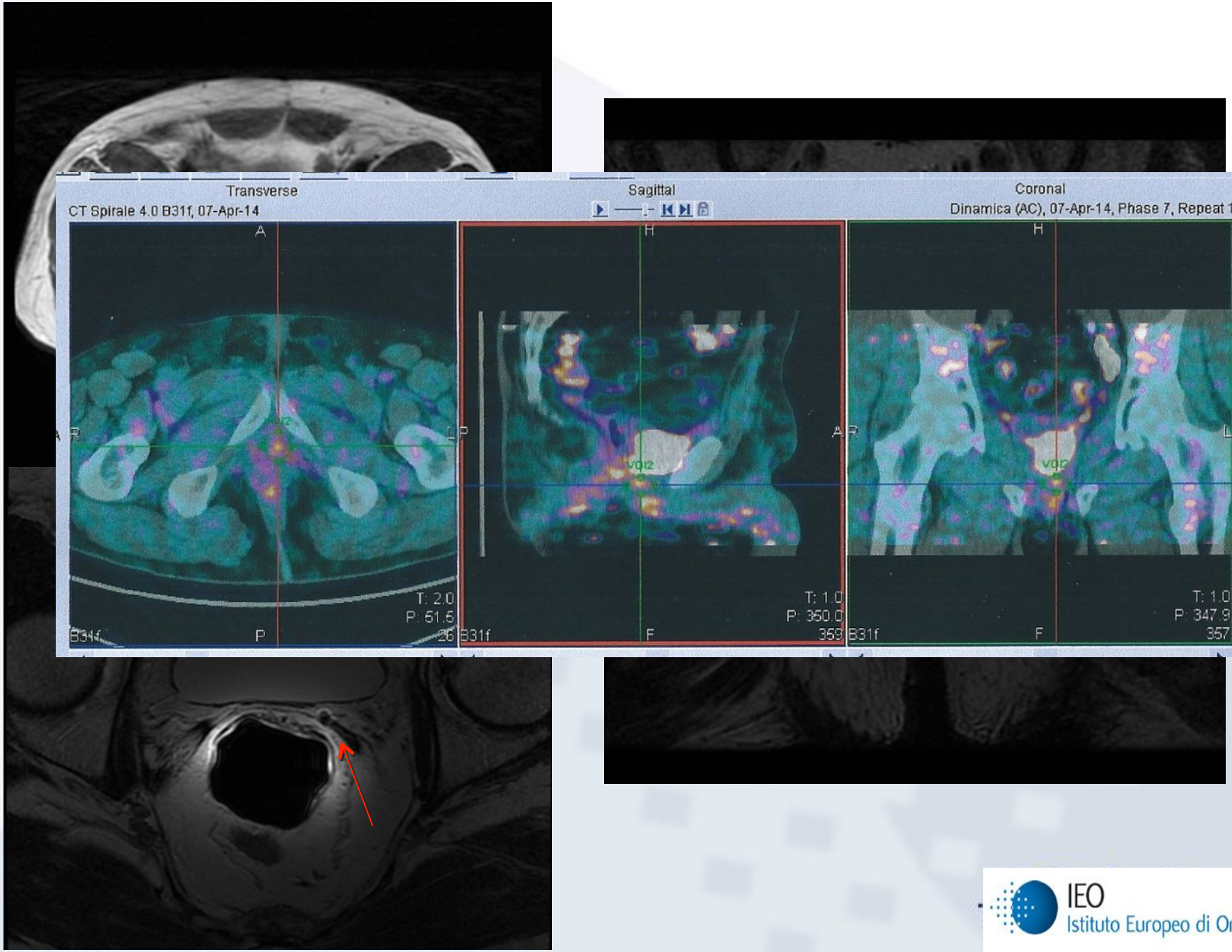

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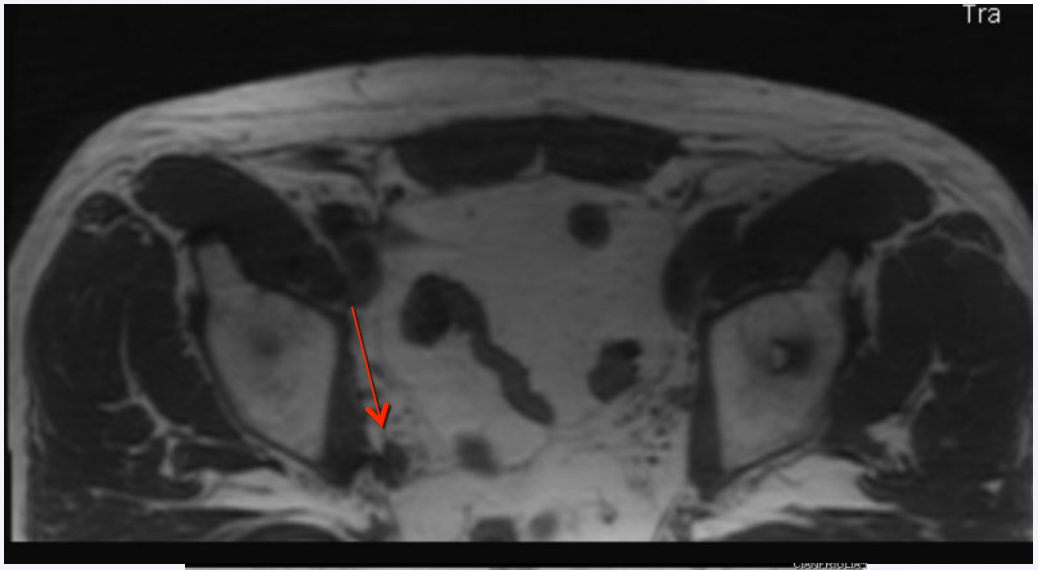
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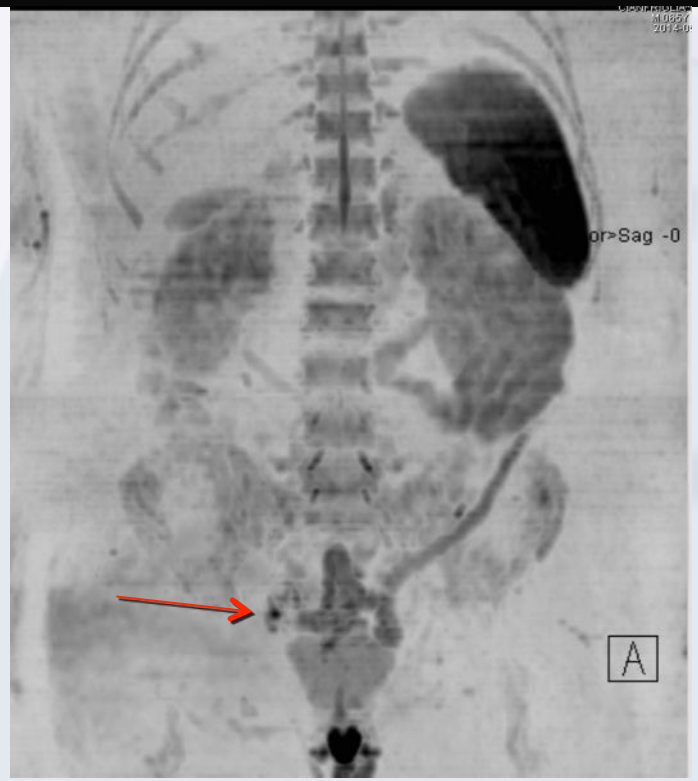
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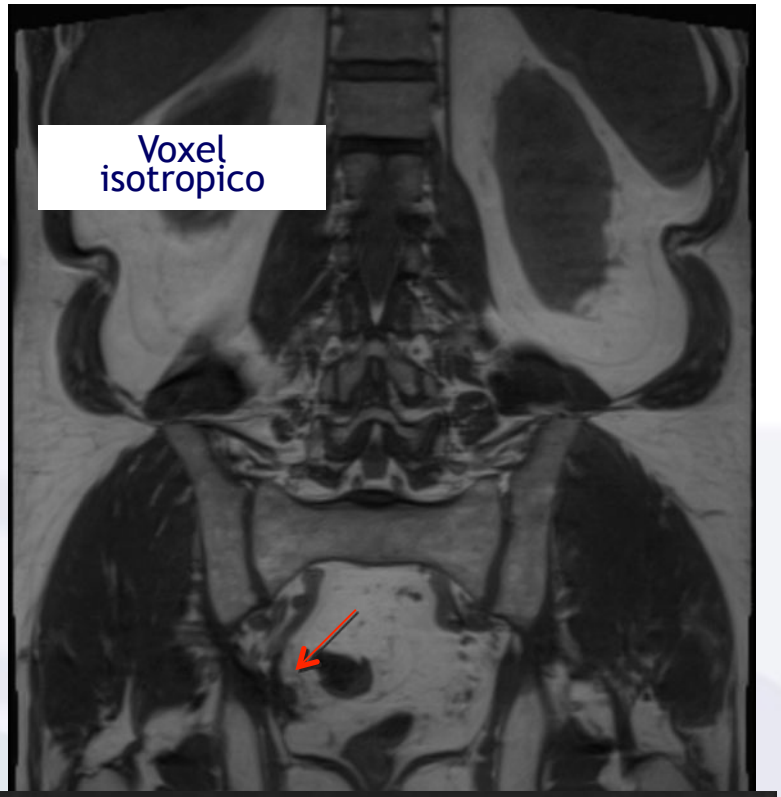
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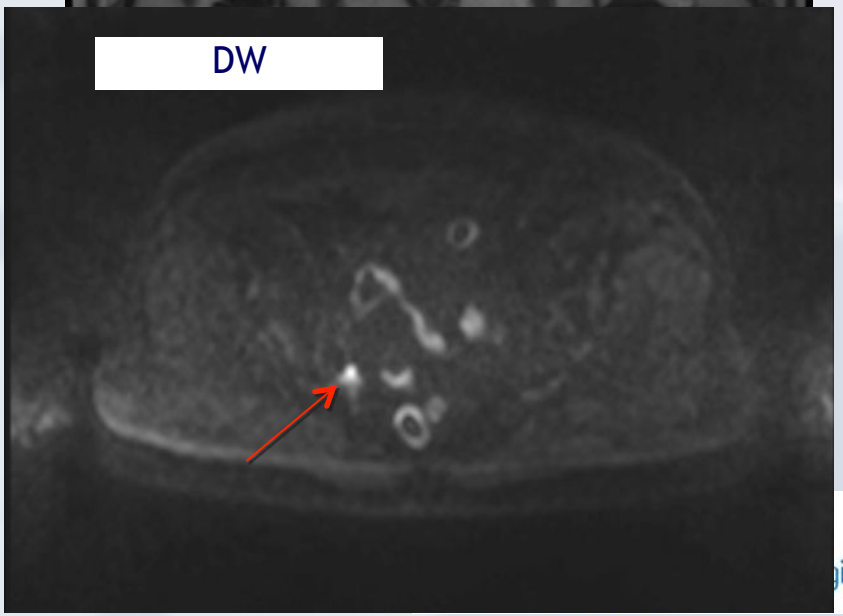
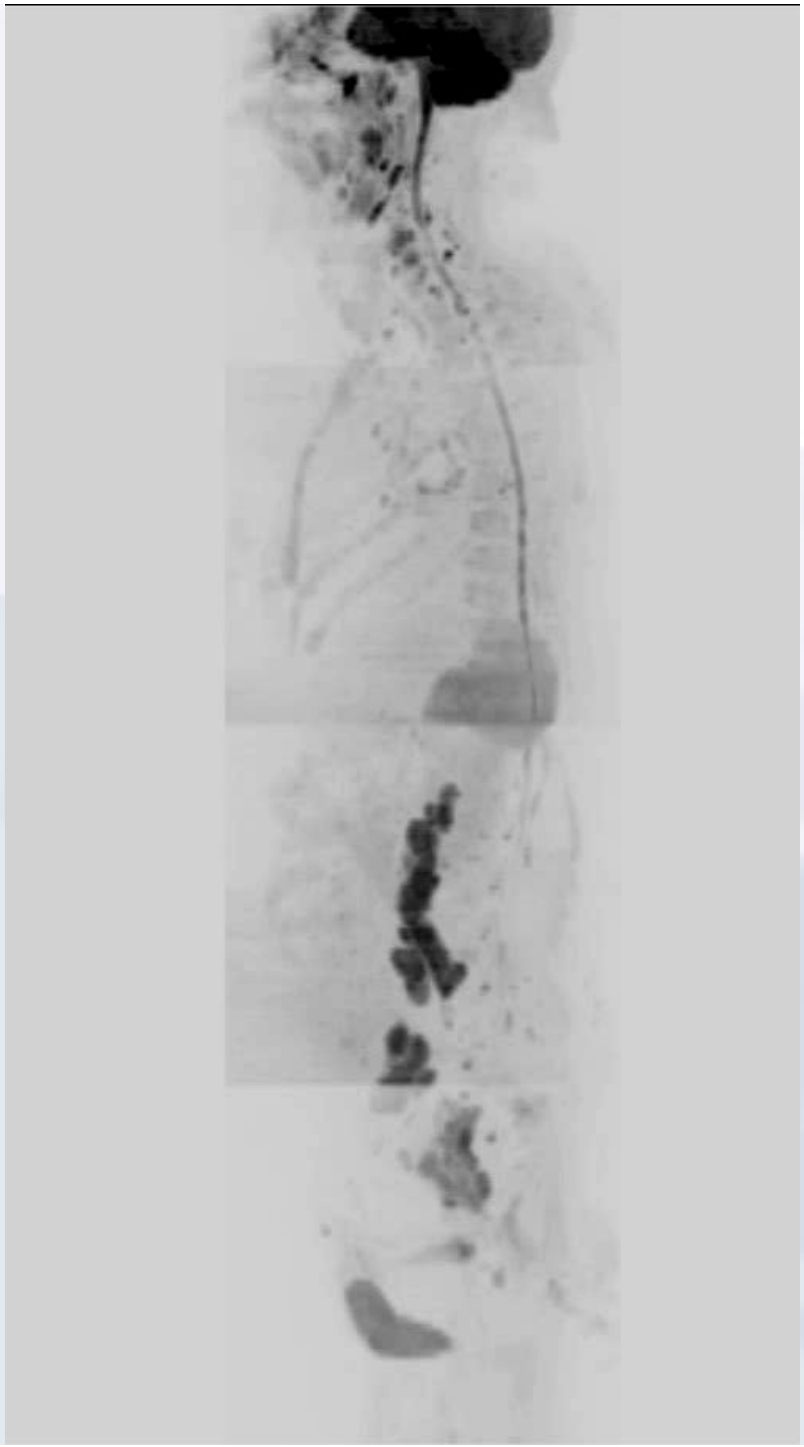

DW

N+

Ricostruzione PET like



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Positive opinions of PET

…18F-choline and 11C-choline PET or PET-CT in the nodal staging of prostate cancer showed a pooled sensitivity of 49.2% and a pooled specificity of 95%

…When a recurrence is suspected after the primary treatment **11C-Choline PET/C** could be suggested as the first procedure in **re-staging** prostate cancer to guide further treatment decisions

…The sensitivity of 11C-Choline PET/CT for to detect the presence of lymph nodal recurrences, local recurrences and bone metastases is

38-85% in patients treated with radical prostatectomy

78-81% in patients treated with definitive RT

Choline PET can be additionally recomanded for patients with a PSA doubling time < 3 months even at low PSA levels.

M. Picchio et al. Radiotherapy and Oncology 96 (2010) 347–350

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Choline PET or PET/CT and Biochemical Relapse of Prostate Cancer

A Systematic Review and Meta-Analysis

Laura Evangelista, MD, PhD, Fabio Zattoni, MD,† Andrea Guttilla, MD,† Giorgio Saladini, MD,* Filiberto Zattoni, MD,† Patrick M. Colletti, MD,‡ and Domenico Rubello, MD§*

Clinical Nuclear Medicine • Volume 38, Number 5, May 2013

TABLE 2. Summary of Studies Included for the Meta-analysis (Patient-Based Analysis)

No.	Author	No. of Patients	Site of Disease	Standard of Reference	Sens. % (95% CI)	Spec. % (95% CI)
1	de Jong et al[39]	22*	All sites	Histological examination	100	83.3 (62–100)
2	Picchio et al[58]	100	All sites	Biopsy/histology and imaging/FUP	80 (69–91)	93.3 (86–100)
3	Scattoni et al[32]	25	Lymph nodes	Histological examination	100	66.6 (29–100)
4	Vees et al[17]	11	Local recurrence	Histological examination	43 (6–71)	50 (10–99)
5	Rinnab et al[35]	50	All sites	Histological examination	94.8 (88–100)	36.3 (8–65)
6	Reske et al[29]	49	Local recurrence	Histological examination	69.9 (54–85)	66.6 (13–100)
7A	Husarik et al[33]	68	All sites	Histological examination	90 (83–97.7)	100
7B	Husarik et al[33]	23	Lymph nodes	Histological examination	100	0
8	Schilling et al[34]	10	Lymph nodes	Histological examination	100	0
9	Pelosi et al[40]	56	All sites	Biopsy/imaging/FUP	82.7 (69–97)	96.2 (89–100)
10	Rinnab et al[18]	15	Lymph nodes	Histological examination	100	0
11	Richter et al[19]	73	All sites	Histological examination	61 (49–72)	100
12	Giovacchini et al[27]	358	All sites	Biopsy/imaging/FUP	85 (79-90)	93 (89–96)
13	Panebianco et al[28]	84	Local recurrence	TRUS biopsy and PSA values	83 (74–91)	63 (29–96)
14	Giovacchini et al[49]	170	All sites	Biopsy/histology and imaging/FUP	86.7 (79–94)	89.5 (83–96)
15	Bertagna et al[30]	45†	Local recurrence	Mapping	60 (30–90)	91 (82–100)
16	Castellucci et al[43]	102	All sites	Biopsy/histology and imaging/FUP	83 (70–95)	100
17	Henninger et al[51]	35	All sites	Biopsy/histology and imaging/FUP	64.3 (47–82)	57.1 (21–94)
18	Schillaci et al[41]	49	All sites	Biopsy/histology and imaging/FUP	91.7 (83–100)	100
19	Marzola et al[59]	233	All sites	Biopsy/histology and imaging/FUP	100	97 (94–100)

90% of patients with a positive choline PET/CT after RP presented histologically proven metastases at the lymph node level.

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Treatment options

salvage surgery

ADT

OBSERVATION

IMRT or SBRT

EURURO-5594; No. of Pages 11

ARTICLE IN PRESS

EUROPEAN UROLOGY XXX (2014) XXX–XXX

Contemporary Role of Salvage Lymphadenectomy in Patients with Recurrence Following Radical Prostatectomy

Firas Abdollah [a,], Alberto Briganti [b], Francesco Montorsi [b], Arnulf Stenzl [c], Christian Stief [d], Bertrand Tombal [e], Hein Van Poppel [f], Karim Touijer [g]*

[a] Vattikuti Urology Institute and VUI Center for Outcomes Research Analytics and Evaluation, Henry Ford Hospital, Detroit, MI, USA; [b] Department of Urology, Vita-Salute University, San Raffaele, Milan, Italy; [c] Department of Urology, Eberhard-Karls-University Tuebingen, Tuebingen, Germany; [d] Department of Urology, Ludwig-Maximilians-University, Klinikum Grosshadern, Munich, Germany; [e] Service d'Urologie, Cliniques universitaires Saint Luc, Université catholique de Louvain, Brussels, Belgium; [f] Department of Urology, Leuven Cancer Institute, Universitair Ziekenhuis Gasthuisberg, Leuven, Belgium; [g] Urology Service, Department of Surgery, Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Table 1 – Performance characteristics of positron emission tomography/computed tomography and magnetic resonance imaging in detecting prostate cancer nodal invasion and/or relapse

Study	Patients, no.	Nature of patients	Site of tumor	Imaging type	Sensitivity, %	Specificity, %	Accuracy, %
De Jong et al. [14]	22	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	100	83.3	90.9
Picchio et al. [17]	100	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	80.0	93.3	86.0
Scattoni et al. [19]	25	Relapse after initial treatment	Lymph nodes	11C-Choline PET/CT scan	100	66.6	92.0
Vees et al. [54]	11	Relapse after initial treatment	Local recurrence	18F-Choline and/or 11C-acetate PET/CT scan	43.0	50	45
Rinnab et al. [36]	50	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	94.8	36.3	82.0
Reske et al. [24]	49	Relapse after initial treatment	Local recurrence	11C-Choline PET/CT scan	69.9	66.6	69.4
Husarik et al. [23]	68	Relapse after initial treatment	All sites	18F-Choline PET/CT scan	90.0	100	91.1
Husarik et al. [23]	23	Relapse after initial treatment	Lymph nodes	18F-Choline PET/CT scan	100	0	78.0
Schilling et al. [28]	10	Relapse after initial treatment	Lymph nodes	11C-Choline PET/CT scan	100	0	70.0
Pelosi et al. [55]	56	Relapse after initial treatment	All sites	18F-Choline PET/CT scan	82.7	96.2	89.2
Rinnab et al. [18]	15	Relapse after initial treatment	Lymph nodes	11C-Choline PET/CT scan	100	0	60
Richter et al. [56]	73	Relapse after initial treatment	All sites	2-Deoxy-2-[F-18]fluoro-D- glucose and 11C-choline PET/CT scan	61	100	62
Giovacchini et al. [50]	358	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	85.0	93.0	89.0
Panebianco et al. [57]	84	Relapse after initial treatment	Local recurrence	18F-Choline PET/CT scan	83.0	63.0	81.0
Giovacchini et al. [58]	170	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	86.7	89.5	88.2
Bertagna et al. [20]	45	Relapse after initial treatment	Local recurrence	11C-Choline PET/CT scan	60.0	91.0	84.0
Castellucci et al. [59]	102	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	83.0	100	94.0
Henniger et al. [60]	35	Relapse after initial treatment	All sites	18F-Choline PET/CT scan	64.3	57.1	62.9
Schillaci et al. [61]	49	Relapse after initial treatment	All sites	18F-Choline PET/CT scan	91.7	100	93.9
Marzola et al. [62]	233	Relapse after initial treatment	All sites	18F-Choline PET/CT scan	100	97.0	99.0
Kitajima et al. [63]	87	Relapse after initial treatment	Local recurrence	11C-Choline PET/CT scan	54.1	92.3	65.5
Kitajima et al. [63]	70	Relapse after initial treatment	Lymph nodes	11C-Choline PET/CT scan	90.0	100	92.9
Kitajima et al. [63]	95	Relapse after initial treatment	Pelvic bone metastasis	11C-Choline PET/CT scan	81.3	98.7	95.8
Mamede et al. [34]	71	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	88.2	98.1	95.8
Ceci et al. [26]	157	Relapse after initial treatment	All sites	11C-Choline PET/CT scan	66.2	0	66.2
Tilki et al. [38]	56	Relapse after initial treatment	All sites	18F-Choline PET/CT scan	39.7	95.8	82.1
Heesakkers et al. [64]	375	Patients with newly diagnosed prostate cancer	Lymph nodes	MRI	34.0	97.0	NA
Lecouvet et al. [44]	100	Patients with newly diagnosed prostate cancer	Lymph nodes	MRI	82	96	NA
Harisinghani et al. [65]	80	Patients with newly diagnosed prostate cancer	Lymph nodes	MRI	100	96	NA
Wang et al. [66]	411	Patients with newly diagnosed prostate cancer	Lymph nodes	MRI	27	98	NA
Eiber et al. [41]	29	Patients with newly diagnosed prostate cancer	Lymph nodes	MRI	86	85	86
Budiharto et al. [43]	36	Patients with newly diagnosed prostate cancer	Lymph nodes	MRI	18.8	97.6	NA

CT = computed tomography; MRI = magnetic resonance imaging; NA = not available; PET = positron emission tomography.

Table 2 – Studies including patients with lymph node–recurrent prostate cancer treated with salvage lymph node dissection

Study	Patients, no.	PSA at SLND, ng/ml, mean	Nodes removed, no., mean	Positive nodes, no., mean	Gleason score	Complete response, %*	Follow-up period, mo, mean	5-yr BCR-free survival, %	5-yr progression-free survival, %	5-yr cancer-specific survival, %
Rinnab et al. [18]	15	1.7	13.9	NA	NA	NA	13.7	NA	NA	NA
Winter et al. [32]	6	2.0	NA	NA	NA	NA	24**	NA	NA	NA
Martini et al. [33]	8	1.6	11.6	1.0	2–6: 25% 7: 37% 8–10: 38%	NA	NA	NA	NA	NA
Schilling et al. [28]	10	10.9	7.1	2.8	2–6: 20% 7: 60% 8–10: 20%	NA	NA	NA	NA	NA
Rigatti et al. [8]	72	3.7	30.6	9.8	2–6: 18% 7: 44.4% 8–10: 37.6%	56.9	39.4	19	34	75
Jilg et al. [7]	52	3.9	23.3	9.7	2–6: 23% 7: 46% 8–10: 31%	46	35.5*	9	26	78
Suardi et al. [53]	162	3.6	24.6	6.1	NA	40.7	29.2	40	47	86
Suardi et al. [52]	59	3.9	29.5	8.9	2–6: 20.3% 7: 44.1% 8–10: 35.6%	59.3	81.1	29.4	52.0	89.1

BCR = biochemical recurrence; NA = not available; PSA = prostate-specific antigen; SLND = salvage lymph node dissection.
* Complete biochemical response was defined as a PSA value <0.2 ng/ml after surgery.
** Median.

- 15.3% lymphorrhea
- 14.5% fever
- 11.2% ileus
- 0.8% uretral injury → 1.6% surgical reinterventation

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Research Article

Extended Salvage Pelvic Lymph Node Dissection in Patients with Recurrent Prostate Cancer

Daniar K. Osmonov, Alexey V. Aksenov, Annkathrin Boller, Almut Kalz, Diana Heimann, Isa Janssen, and Klaus-Peter Jünemann

Department of Urology and Pediatric Urology, University Hospital Schleswig-Holstein, Campus Kiel, Arnold-Heller-Straße 7, 24105 Kiel, Germany

TABLE 1: Results after salvage treatment in all three groups.

1- Extended salvage PLND in patients with LN metastasis and BCR of PCa is a valid and safe therapy option.

2- Extended salvage PLND is not a curative treatment option but it increases the duration of ADT sensibility as well as the BCRF and CSS.

Early (intraoperative or 3 days after surgery)	
Bleeding	2 (4.9%)
Ureteral injury	1 (2.4%)
Late (more than 3 days after surgery)	
Lymphocele	2 (4.9%)
Ureteral stricture	1 (2.4%)
Rectovesical fistula	1 (2.4%)

primary RT can increase the risk of such complications and can lead to intraoperative difficulties due to the tissue-changing properties of radiation

Advances in Urology Volume 2014 (2014), Article ID 321619, 8 pages

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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]

At SBRT	
PSA (ng/mL)	
Median	6.59
Range	0.34-72.9
Age (years)	
Median	67
Range	54-78
Location of lesions, n (%)	
Bones	
Axial	18 (37)
Nonaxial	9 (18)
Lymph nodes	
Pelvic	15 (31)
Extrapelvic	7 (14)

Primary end point: ADT-FS

All pts underwent a PET/CT

Clinical Genitourinary Cancer, Vol. 11, No. 1, 27-32 © 2013 E

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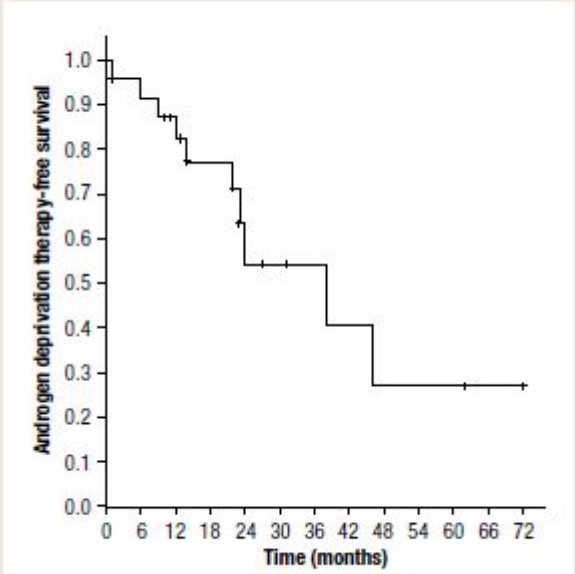
Figure 3 Kaplan-Meier Curve Representing Androgen Deprivation Therapy-Free Survival



Repeated salvage SBRT is feasible, well tolerated and defers palliative ADT with a median of 38 months in patients with limited bone or lymph node PCa metastases

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11C-Choline PET/CT

as a guide to radiotherapy treatment planning

Partial prostate re-irradiation or isolated lymph node irradiation

Robotic stereotactic radiotherapy

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

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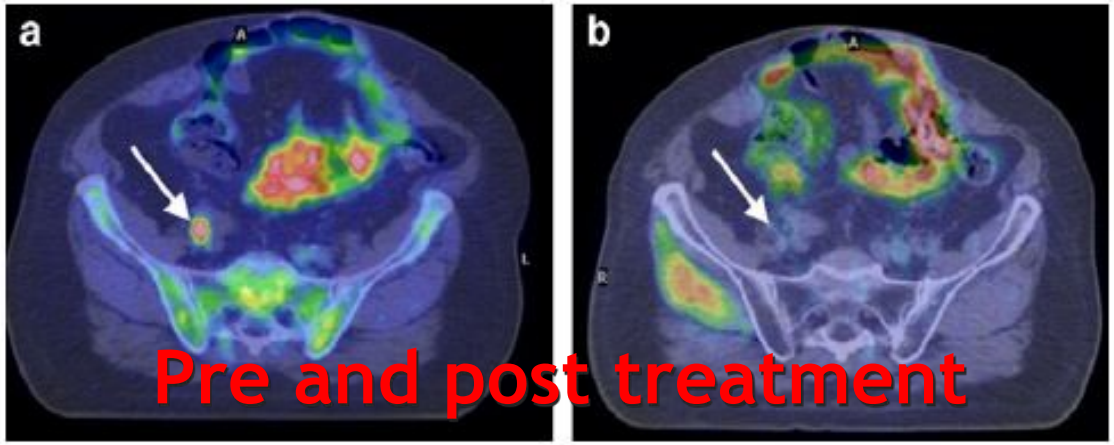

Pre and post treatment

Mean follow-up of 18.6 months:

8/14 NED
5/14 AWD
1/14 died

Radiotherapy and Oncology 93 (2009) 14–17

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11C-Choline PET/CT

as a guide to radiotherapy treatment planning

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

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- *16/34 pts*
- interval between first diagnosis of prostate cancer and diagnosis of recurrent disease of greater than 23 months
- CKRT: 33 Gy given in 3 consecutive daily fractions
- The median follow-up period was 16.9 months (range, 3-35.2 months)
- A complete biochemical response was observed in 60% pts treated with radiotherapy alone.

excellent in-field tumor control and a low toxicity profile

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

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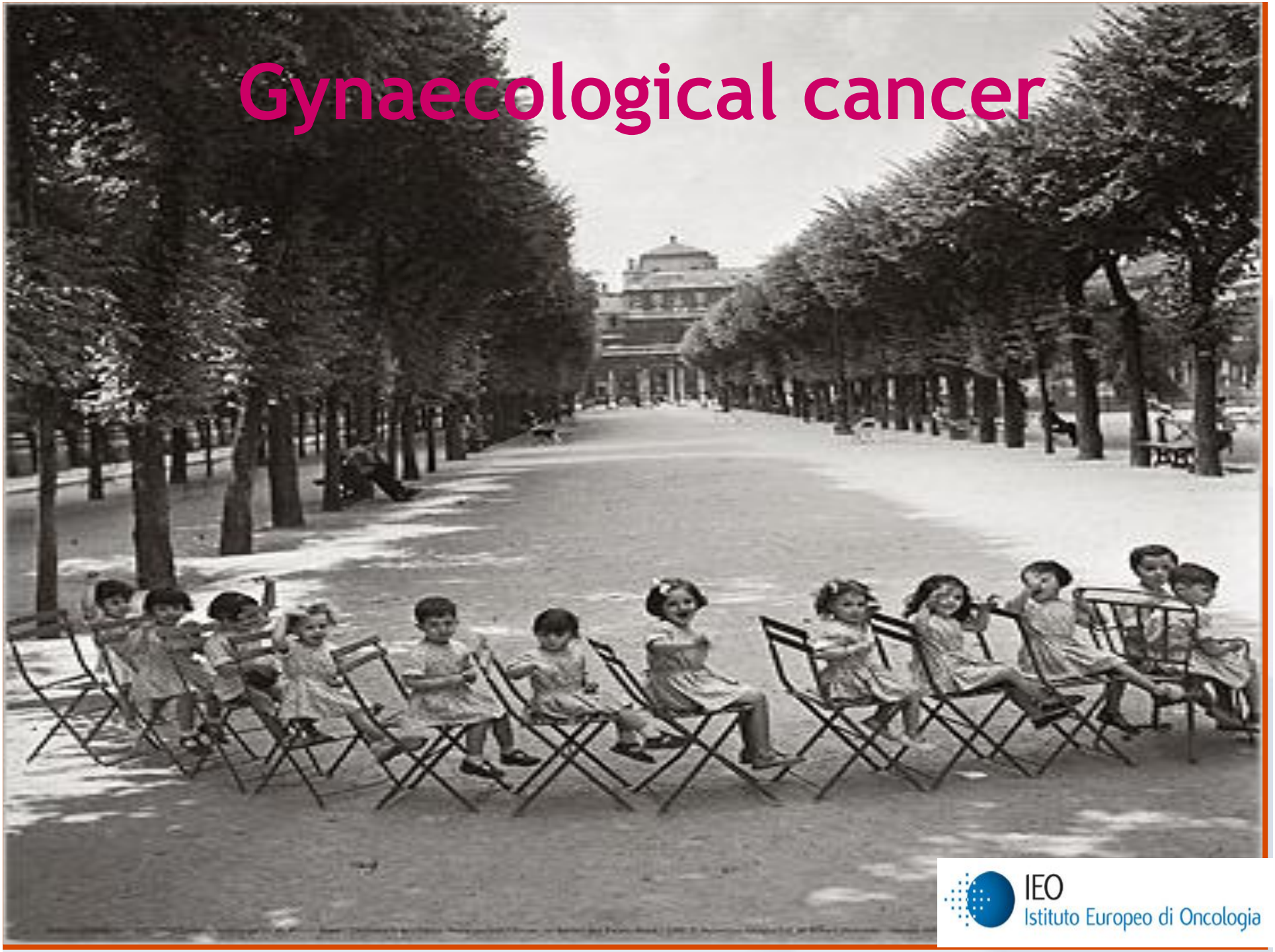
Gynaecological cancer



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Gynaecological experiences

Table 4
SBRT used for gynecologic malignancies or sites of disease at the University of North Carolina.

Pt. no	Age	Histology	Clinical setting	DFI (m.)	RT (Gy)	SBRT (Gy/fx)	F/u (m.)	LR control[a]	Systemic failures[b]	Status	Toxicity[c]
Pelvic and periaortic nodes											
1	63	Endometrial[d]	PAN recurrence	29	–	30/5	10	–	–	NED	None
2	56	Endometrial[d]	PAN recurrence	18	45	25/5	18	–	–	NED	None
3	77	Endometrial[d]	PAN recurrence	22	46	20/4	6	Unknown	Unknown	Dead	Acute grade I diarrhea/loose stools and grade 2 abdominal pain
4	51	Endometrial[d]	Pelvic node recurrence	72	45	25/5	5	–	–	NED	Acute grade I abdominal pain
5	44	Cervix[e]	PAN recurrence	35	45	30/5	3	–	Malignant pleural effusion @1 m.	DOD	None
6	33	Cervix[e]	PAN recurrence	35	–[f]	30/5	25	New PAN @7 m.	–	DOD	None
7	40	Cervix[e]	Pelvic node at initial dx		54	12/3	24			NED	None
8	77	Ovarian[d]	Isolated PAN	42	45	25/5	19	–	–	NED	None
9	50	Ovarian[d]	Isolated PAN	72	–	30/5	33	New PAN @10 m.	Porta hepatis nodes @10 m.	AWD	None
Oligometastatic disease											
10	59	Uterine stromal sarcoma	T8, T11 bone lesions	11	30	25/5	0.3	Unknown	Brain mets. @10 days	DOD	None
11	65	Cervix[e]	Solitary lung lesion	23	–	54/3	21	–	New lung nodules @2 m.	AWD	None
Substitute for brachytherapy											
12	89	Endometrial[d]	Medically inoperable, could not tolerate brachytherapy	–	48.8	20/5	8	–	Unknown	Dead	Late grade 3 rectal bleeding
13	67	Vaginal[e]	Periurethral location	–	45	25/5	22	–	Lung mets. @17 m.	DOD	Acute grade 2 radiation cystitis
14	62	Vaginal[e]	Prior cervical ca. in 1981. Now upper vaginal cuff disease.	–	40	25/5	7	@5 months	–	DOD	None
15	77	Urothelial carcinoma of the bladder	Recurrent disease at vaginal apex after prior cystectomy	6	45	16/4	12	–	–	NED	None
16	51	Cervix[e]	Recurrent disease within vaginal cuff after prior chemoradiation	34	–	25/5	10	–	Liver mets. @2 m.	DOD	None

DFI: disease-free interval before SBRT. F/u: follow-up. RT: conventional radiotherapy. Fx: fractions. LR: locoregional. Mets.: metastases. NED: no evidence of disease. AWD: alive with disease. LR: locoregional. DOD: dead of disease.

[a] Local control defined as progressive disease by RECIST v1.1 criteria using subsequent CT or PET-CT for patients 1–11. Patient 12 had a negative transvaginal ultrasound and normal examination shortly before death. Patients 13–16 were assessed by physical examination. Patients 6 and 9 developed new PANs which were distinct from those treated with SBRT. "–" signifies LR control. When imaging or follow-up examination not available, "unknown" is designated. Time to failure after SBRT is designated as @× months.

[b] "–"signifies absent distant metastases on subsequent CT or PET-CT imaging. When subsequent imaging is not available, "unknown" is designated.

[c] RTOG Acute Radiation Morbidity Scoring Criteria used for symptoms occurring from day 1 to day 90 following SBRT. RTOG/EORTC Late Radiation Morbidity Scoring Schema used for symptoms occurring on day 91 and afterwards.

[d] Adenocarcinoma.

[e] Squamous cell carcinoma.

[f] Patient 6 received prior conventional RT to the PAN region in 2003. SBRT performed in 2008 for an isolated recurrence.

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In review

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Stereotactic body radiotherapy (SBRT) versus volumetric modulated Rapidarc™ radiotherapy (RA-IMRT) in lymph-node recurrence of gynaecological malignancies

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From January 2010 to September 2011, 15 patients affected by isolated lymph nodes recurrence of gynaecological cancer underwent salvage radiotherapy .Two different radiotherapy techniques were used in this study: RA-IMRT or SBRT

Table 1. Patient, tumor and treatment characteristics (N=15 patients, n=16 lymph nodes)

Characteristics	All patients N=15
Age (years), at the treatment	
Mean	62.8
Range	40 - 79
Primary diagnosis (N=15 patients)	
Ovarian cancer	9
Cervical cancer	4
Endometrial cancer	1
Uterine tube cancer	1
Previous RT	3*
RT treatment (patients/lymph nodes)	
RA-IMRT	6/6
SBRT	9/10

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The dose for the hypofractionated schedule was :

8/10 Gy x 3 fr = 24/30 Gy

EQD2=36/50 Gy

Table 2. Radiotherapy details

Technique	Site/n°		RT total dose and dose/fraction	Number of fraction	Duration of RT (in days)
RA-IMRT	Chest wall	1	60 (2)	30	45
	Hepatic hilus	1	50 (2)	25	36
	Common iliac lymph node	1	50 (2)	25	36
	Pararectal	1	55.8 (1.8)	31	44
	Presacral	1	56 (2)	28	39
	Perigastric	1	54 (1.8)	30	43
SBRT	Para-aortic	7	25 (8)^	3^	5^
	Supraclavicular	1	24 (6)	4	8
	Cardiophrenic	1	30 (10)	3	5
	Lung hilar lymph node	1	32 (8)	4	8

Legend: RA-IMRT: volumetric modulated Rapidarc radiotherapy; SBRT: stereotactic body radiotherapy; ^ - median dose Gy (Gy/fraction), median number fraction and median days RT

Patients/nodes	RA-IMRT	SBRT
Acute toxicity (for patients)	5	8
Yes	2	1
Follow-up duration (months)		
Median (range)	26 (10-36)	33.7 (22-36)
Response to treatment		
Radiological (CT) and/or [^{18}F]FDG-PET/CT :		
Evaluable (nodes)	5	10
Local control (for nodes)	5 (100%)	9 (90%)
Non local control	0	1 (10%)
Non evaluable (NE)	1	0
Complete response (for patients)	2 (40%)	5 (55%)
Progression of disease in other sites	2 (40%)	4 (44%)
Died for progression of disease	2	0
Non evaluable (NE)	0	0
Overall survival rate (for patients)	3 (60%)	9 (100%)

Legend: computer tomography (CT) , 18-fluoro-deoxy-glucose positron emission tomography/CT ([^{18}F]FDG-PET/CT); volumetric modulated Rapidarc radiotherapy (RA-IMRT), stereotactic body radiotherapy (SBRT)

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Our experience : 2010-2013

Material and Methods

- 37 pts treated for 1 or 2 localisation of ovarian cancer
- 7 pts treated for M+ (bone or brain)

Radiotherapy Technique (SBRT vs IMRT)

- 28 pts treated with **SBRT**: 3-5 fractions of 8-10 Gy/fr (only for liver and lung with a total dose of 36-45 Gy in 3 fracions)
- 9 pts treated with **IMRT Trilogy Rapidarc** (50-55 Gy in 25-28 fraction)

Results after a mean follow-up of 13 months

- **28 LC**
- 8 lost in f-up
- 1 PD in the site of RT

- **14 NED**
- 1 died
- 12 PD
- 10 no follow-up

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Our constraints of doses

Serial Tissue	Volume (mL)	Volume Max (Gy)	Max Point Dose (Gy)	Endpoint (≥Grade 3)
THREE-FRACTION TREATMENT				
Optic pathway	<0.2	15 (5 Gy/fx)	19.5 (6.5 Gy/fx)	Neuritis
Cochlea			20 (6.67 Gy/fx)	Hearing loss
Brainstem	<1	18 (6 Gy/fx)	23 (7.67 Gy/fx)	Cranial neuropathy
Spinal cord	<0.25	18 (6 Gy/fx)	22 (7.33 Gy/fx)	Myelitis
	<1.2	11.1 (3.7 Gy/fx)		
Cauda equina	<5	21.9 (7.3 Gy/fx)	24 (8 Gy/fx)	Neuritis
Sacral plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Esophagus*	<5	21 (7 Gy/fx)	27 (9 Gy/fx)	Stenosis/fistula
Ipsilateral brachial plexus	<3	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Neuropathy
Heart/pericardium	<15	24 (8 Gy/fx)	30 (10 Gy/fx)	Pericarditis
Great vessels	<10	39 (13 Gy/fx)	45 (15 Gy/fx)	Aneurysm
Trachea and ipsilateral bronchus*	<4	15 (5 Gy/fx)	30 (10 Gy/fx)	Stenosis/fistula
Skin	<10	22.5 (7.5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Stomach	<10	21 (7 Gy/fx)	24 (8 Gy/fx)	Ulceration/fistula
Duodenum*	<5	15 (5 Gy/fx)	24 (8 Gy/fx)	Ulceration
Jejunum/ileum*	<5	16.2 (5.4 Gy/fx)	27 (9 Gy/fx)	Enteritis/obstruction
Colon*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Colitis/fistula
Rectum*	<20	20.4 (6.8 Gy/fx)	30 (10 Gy/fx)	Proctitis/fistula
Bladder wall	<15	15 (5 Gy/fx)	30 (10 Gy/fx)	Cystitis/fistula
Penile bulb	<3	21.9 (7.3 Gy/fx)	42 (14 Gy/fx)	Impotence
Femoral heads (right and left)	<10	21.9 (7.3 Gy/fx)		Necrosis
Renal hilum/vascular trunk	<2/3 volume	18.6 (6.2 Gy/fx)		Malignant hypertension

Parallel Tissue	Critical Volume (mL)	Critical Volume Dose Max (Gy)	Endpoint (≥Grade 3)
Lung (right and left)	1,500	10.5 (3.5 Gy/fx)	Basic lung function
Lung (right and left)	1,000	11.4 (3.8 Gy/fx)	Pneumonitis
Liver	700	17.1 (5.7 Gy/fx)	Basic liver function
Renal cortex (right and left)	200	14.4 (4.8 Gy/fx)	Basic renal function

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Take home message

- Technological evolution in radiotherapy will probably offer even more precise and fast delivery opportunities

- SBRT represent promising non-invasive treatment options for oligo-recurrent with an excellent tumor control and very good toxicity profile: “RT= virtual surgery”

- With the RT it is possible to delay the start of systemic therapies

- Data on best fractionation schedules in term of efficacy and toxicity will be available from ongoing studies in selected organs/treatment sites.

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"If you can't see it, you can't hit it,

and if you can't hit it, you can't cure it"

(credited to the Canadian medi[illegible] Johns)

Grazie per l' attenzione

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