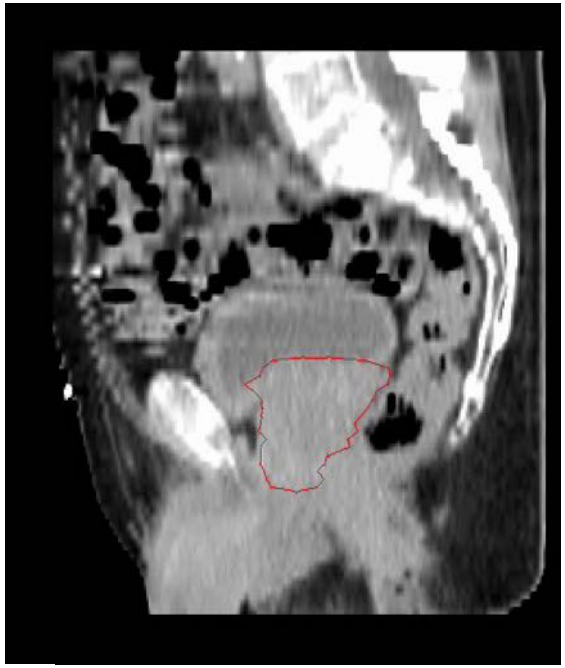
Esperienze in IGRT: US-guided e altre modalità

Sara Bartoncini

AOU Città della Salute e della Scienza di Torino
Radioterapia U
University of Turin

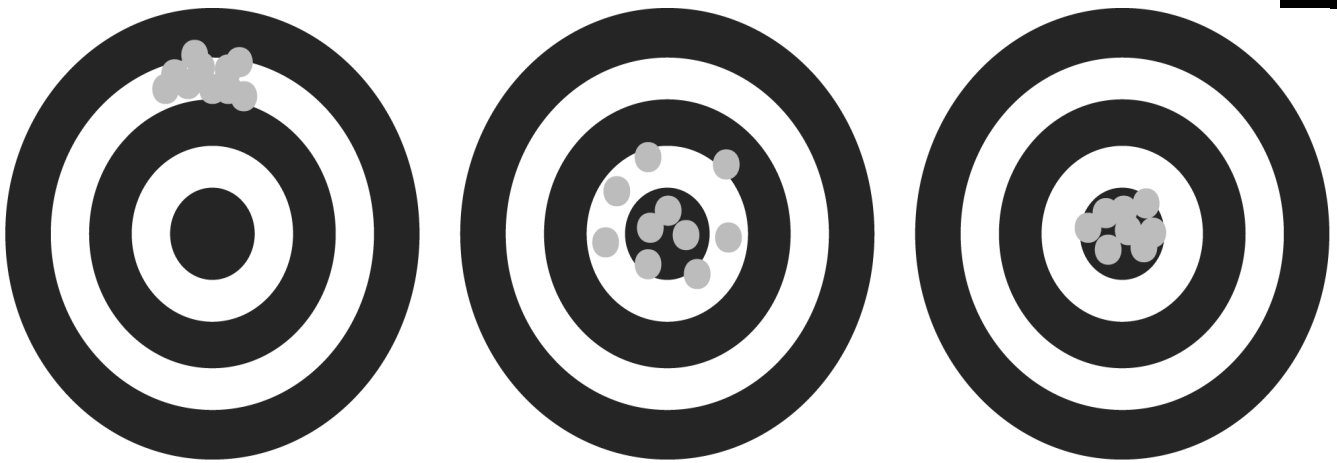
RATIONALE FOR IGRT

Set-up error
Organ motion



Highly conformal radiation techniques → Geographical miss

Dose (per – fraction) escalation → PTV margin reduction



Precise, not accurate
(IMRT without IGRT)

Accurate, but not precise
(wide margin radiotherapy)

Precise and accurate
(IMRT with IGRT)

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From CTV to PTV

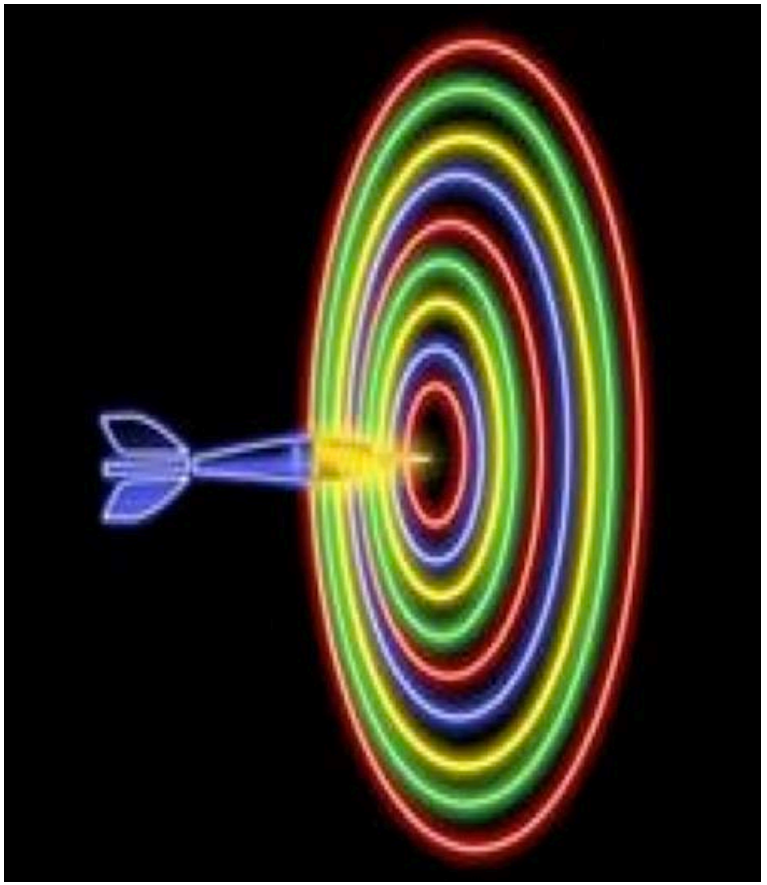
Internal Margin for organ motion

Intra-fraction motion

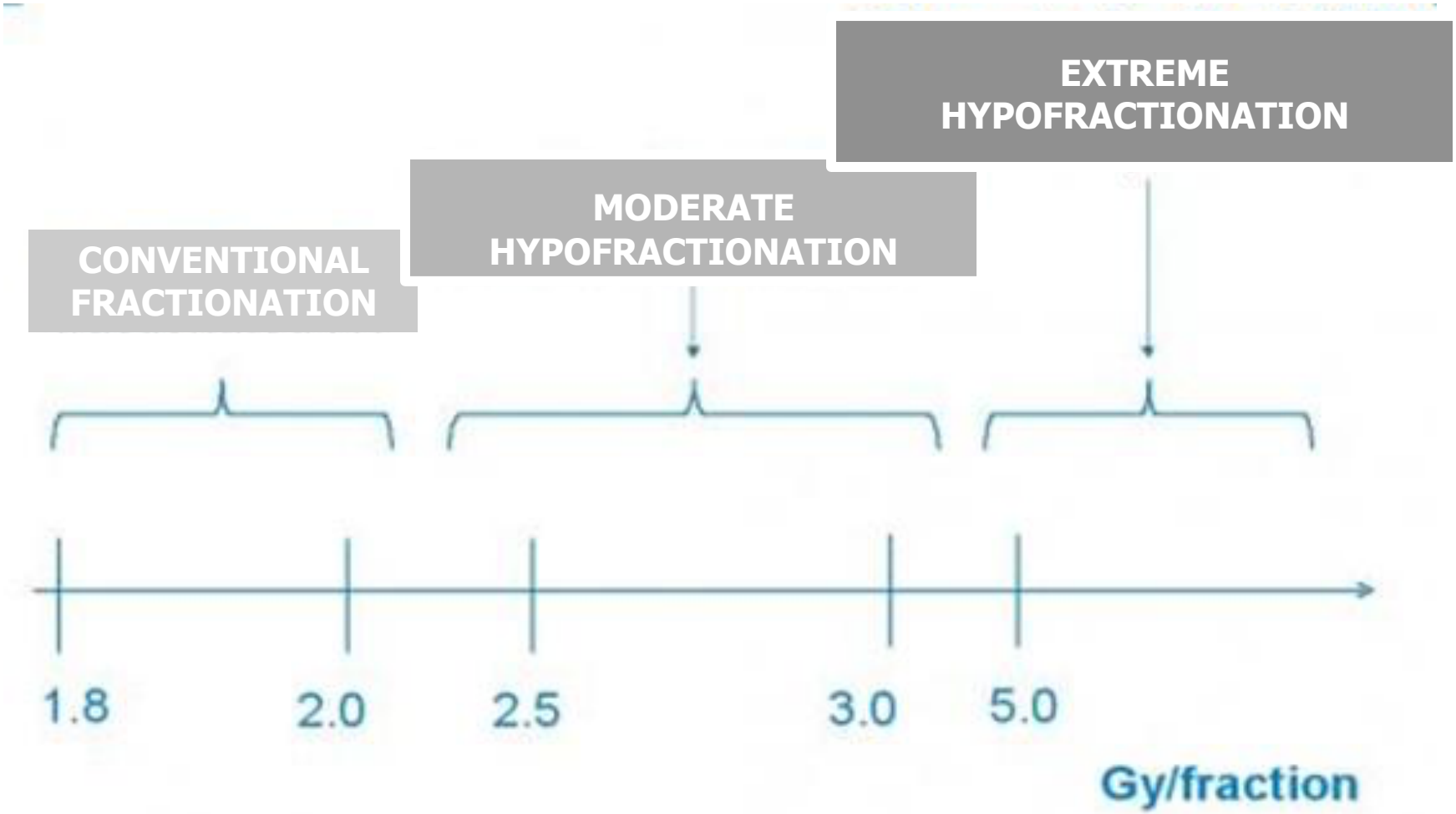
- Respiratory
- Bowel movement
- Bladder filling

Inter-fraction motion

- Bowel filling
- Bladder filling
- Setup Errors



ADVANCES IN RADICAL RADIOTHERAPY



HYPOFRACTIONATION

Cancer Treatment Reviews 39 (2013) 728–736

Contents lists available at SciVerse ScienceDirect

Cancer Treatment Reviews

journal homepage: www.elsevierhealth.com/journals/ctrv

Anti-Tumour Treatment

Systematic review of hypofractionated radiation therapy for prostate cancer

Nicholas G. Zaorsky [a,*], Nitin Ohri [a], Timothy N. Showalter [b], Adam P. Dicker [a], Robert B. Den [a]

[a] Department of Radiation Oncology, Jefferson Medical College & Kimmel Cancer Center, Thomas Jefferson University, 111 S, 11th Street, Bodine Center for Cancer Treatment, Philadelphia, PA 19107, USA
[b] Department of Radiation Oncology, University of Virginia School of Medicine, Charlottesville, Virginia

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Review – Prostate Cancer

A Systematic Review of Hypofractionation for Primary Management of Prostate Cancer

Bridget F. Koontz [a,], Alberto Bossi [b], Cesare Cozzarini [c], Thomas Wiegel [d], Anthony D'Amico [e]*

Curr Oncol Rep (2017) 19: 30
DOI 10.1007/s11912-017-0584-7

GENITOURINARY CANCERS (DP PETRYLAK AND JW KIM, SECTION EDITORS)

The Role of Hypofractionated Radiotherapy in Prostate Cancer

Linus C. Benjamin [1] · Alison C. Tree [1,2] · David P. Dearnaley [1,2]

3 systematic reviews, 9 randomized controlled trials

6357 patients randomized to CF or MH

MH **well tolerated and as clinically effective** as CF

Superiority randomized studies		
Arcangeli [30]	LR/IR 24% HR 76%	CFRT
Hoffman [29]	LR 28% IR 71% HR 1%	IG-IMRT
Pollack [31]	IR 36% HR 64%	IMRT
HYPRO [2–17, 18••, 19–21, 22•]	IR 27% HR 73%	CFRT
Non-inferiority randomized studies		
RTOG 0415 [23•]	LR	IMRT 79–80% CFRT 20–21%
PROFIT [24•]	IR	IGRT
		IGRT
CHHiP [18••, 19, 27]	LR 15% IR 73% HR 12%	IMRT +/− IGRT

SEVERE HYPOFRACTIONATION

Original research article

SBRT and extreme hypofractionation: A new era in prostate cancer treatments?

Table 1 – Stereotactic radiotherapy in prostate cancer.

Study	Treatment	# of patients	Risk group(s)	Median follow-up (months)	Late Grade 3 GU toxicity	Late Grade 3 GI toxicity	FFBF
Gantry-based systems							
Madsen et al.[52]	33.5 Gy in 5 fx	40	Low	41	None	None	90% 4-years actuarial
Boike et al.[53]	45–50 Gy in 5 fx	45	Low and int	30, 18, 12	4%	2% plus 1 Grade 4	100%
Alongi et al.[54]	35 Gy in 5 fx	40	Low and int	11	None	None	–
Loblaw et al.[56]	35 Gy in 5 fx Once a week	84	Low	55	1%	None	98% 5-year
Cyberknife							
King et al.[45]	36.25 Gy in 5 fx	69	Low	32	3.5%	None	97%
Friedland et al.[40]	35 Gy in 5 fx	112	Low, int, and high	24	< 1%	None	98%
Katz et al.[43]	35–36.25 Gy in 5 fx	304	Low, int and high	48	2%	None	97, 93, 75% 4-year actuarial
Freeman et al.[47]	7–7.25 Gy in 5 fx	41	Low	60	< 1%	None	93% 5-year actuarial
Bolzicco et al.[42]	35 Gy in 5 fx	100	Low, int and high	36	None	None	96%
McBride et al.[51]	36.25–37.5 Gy in 5 fx	45	Low	44	< 1%	None	100%
Ju et al.[50]	35–36.25 Gy in 5 fx	41	Int	21	None	None	97.56%
Chen et al.[49]	35–36.25 Gy in 5 fx	100	Low, int and high	26	None	None	99%
Kang et al.[37]	32–36 Gy in 4 fx	44	Low, int and high	40	None	None	100%, 100%, 90.9%
Oliai et al.[48]	37.5 Gy vs. 35–36.25 Gy in 5 fractions	70	Low, int and high	27–37	4%	None	100%, 95%, 77.1% 3-years
King et al.[22]	36.25 Gy in 4–5 fractions	1100	Low, int and high	36	–	–	93% 5-years

FFBF: free from biochemical failure; int.: intermediate; GU: genitourinary; GI: gastrointestinal.

Phase I-II data encouraging

Phase III data is eagerly awaited

(HYPO trial, PACE B)

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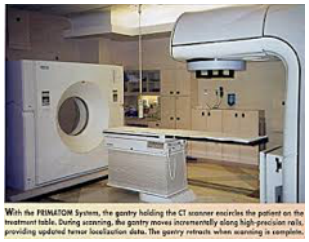
IGRT TECHNOLOGIES

Ultrasound

KV Radiographic

Portal imaging

Markers



Siemens PRIMATON

KV CT

TomoTherapy Hi-Art

MV CT

Elekta Synergy

Varian OBI

KV and MV Cone-beam CT

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Gold seeds

US Clarity

Elekta Axesse

BRT

US Autoscan

RayPilot

2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018

STOP

Naburen

POP II

SBRT

HYPOP I

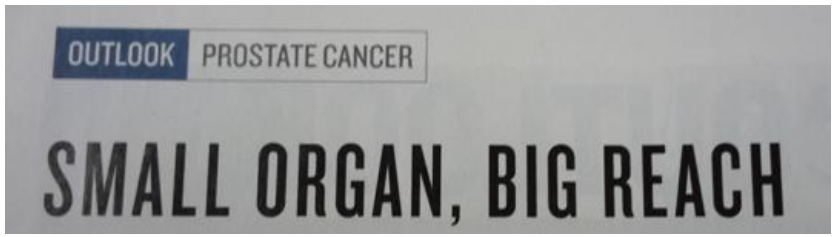
POP III

START

EUREKA

ProsIT

HEAT



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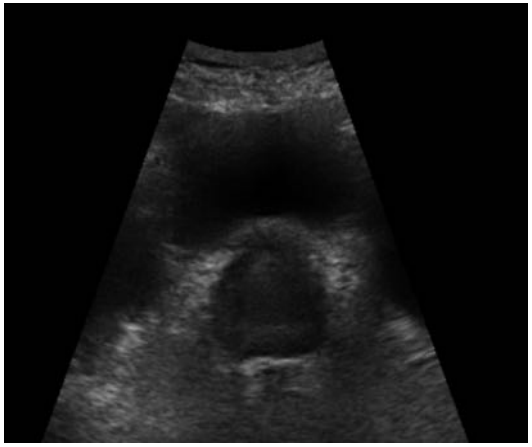
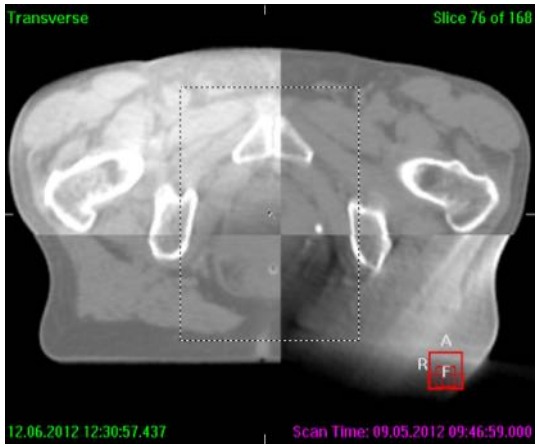
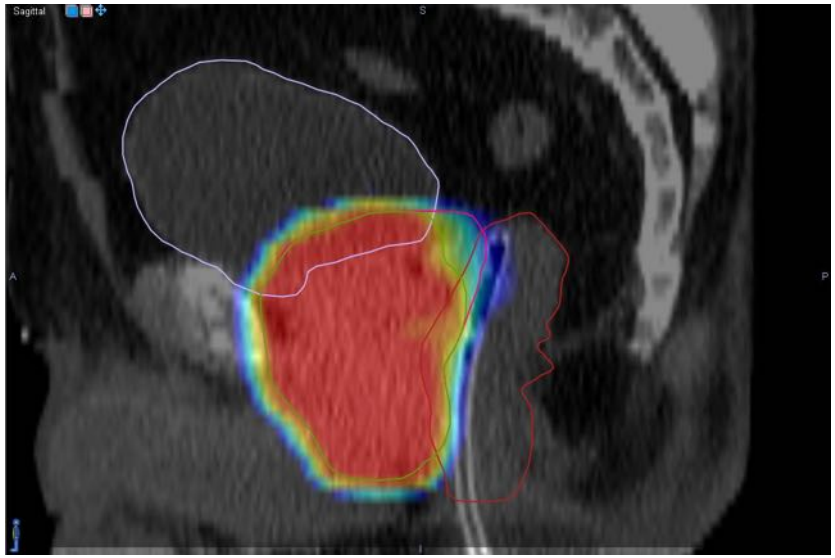
MODERATE HYPOFRACTIONATION

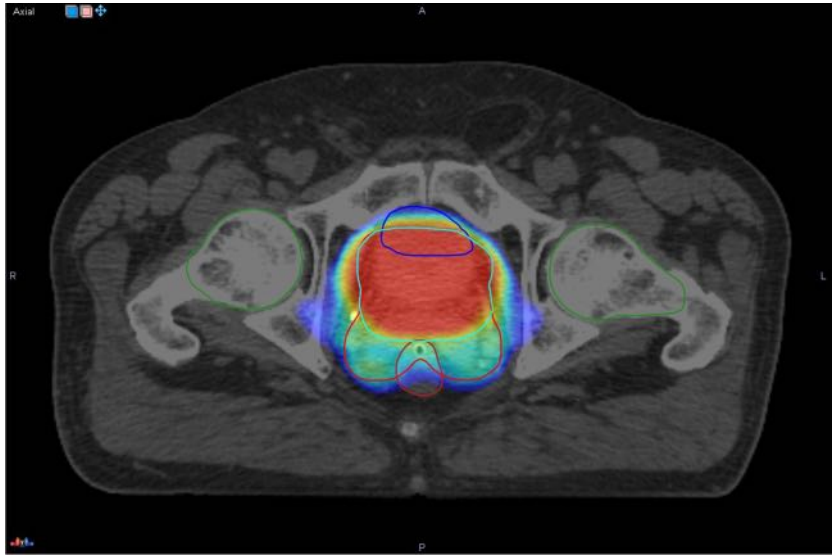
- **Intermediate risk**
- **Schedule:** 70,2 Gy/26 fractions
- IMRT-VMAT
- **IGRT- Daily US acquisition or CBCT**





SEVERE HYPOFRACTIONATION





- ❑ Low-risk
- ❑ Schedule: 36.25 Gy/5 fractions
- ❑ IMRT-VMAT plan
- ❑ **IGRT-Daily ultrasound acquisition**

- 29 patients underwent SBRT
- 27 patients selected for this analysis

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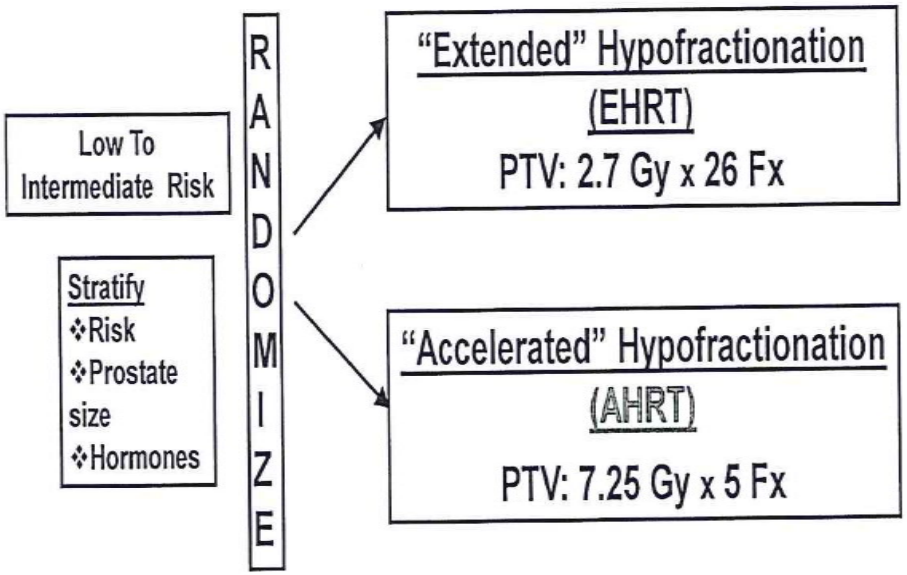
HEAT STUDY

A **Phase III trial** of Radiation Hypofractionation via Extended versus Accelerated Therapy **(HEAT)** for prostate cancer



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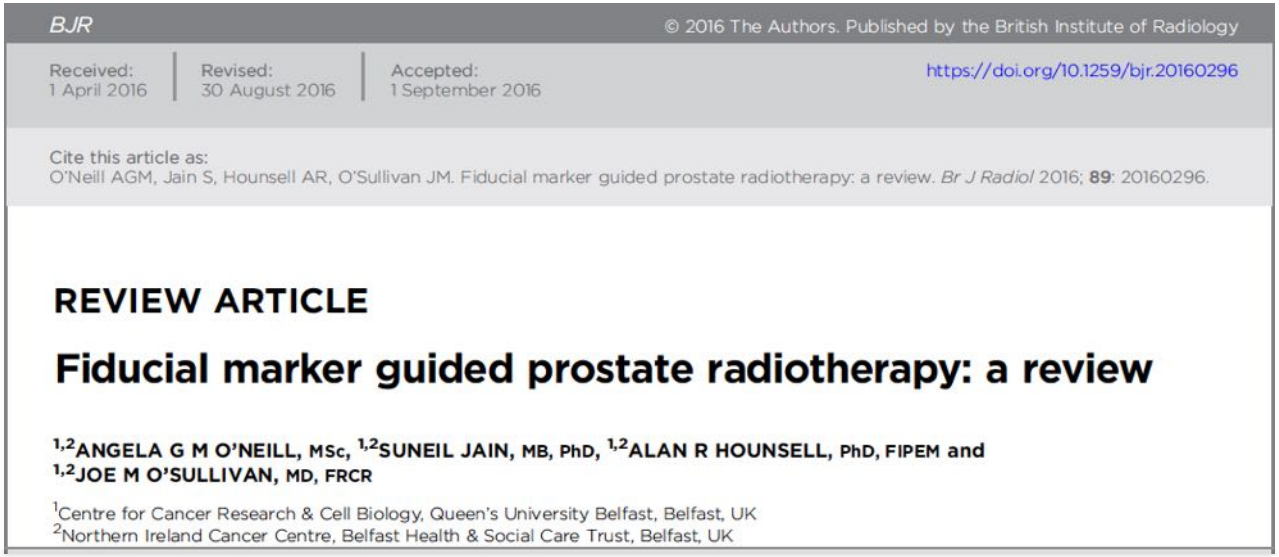
FIDUCIAL MARKERS



BJR

Received: 1 April 2016 | Revised: 30 August 2016 | Accepted: 1 September 2016
https://doi.org/10.1259/bjr.20160296

Cite this article as:
O'Neill AGM, Jain S, Hounsell AR, O'Sullivan JM. Fiducial marker guided prostate radiotherapy: a review. *Br J Radiol* 2016; **89**: 20160296.

REVIEW ARTICLE

Fiducial marker guided prostate radiotherapy: a review

[1,2]ANGELA G M O'NEILL, MSc, [1,2]SUNEIL JAIN, MB, PhD, [1,2]ALAN R HOUNSELL, PhD, FIPEM and [1,2]JOE M O'SULLIVAN, MD, FRCR

[1]Centre for Cancer Research & Cell Biology, Queen's University Belfast, Belfast, UK
[2]Northern Ireland Cancer Centre, Belfast Health & Social Care Trust, Belfast, UK

- Position of prostate, reflect prostate motion or deformation
- Changes in rectal/bladder volume and SV motion are not detected
- Combination of FM and soft-tissue analysis is the most effective approach
- Marker migration is minimal
- Implantation wel tolerated, but surgical techniques and toxicity data require standardization

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EXPERIENCE WITH GOLD SEED FIDUCIALS

Radiol med
DOI 10.1007/s11547-012-0797-7

RADIOTHERAPY
RADIOTERAPIA

Tracking target position variability using intraprostatic fiducial markers and electronic portal imaging in prostate cancer radiotherapy

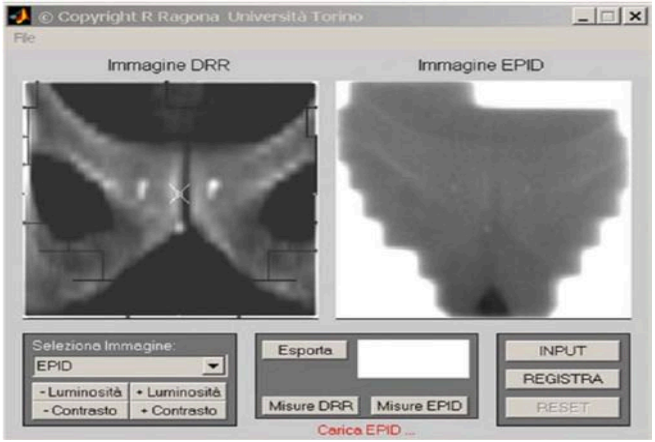


Table 2 Systematic (Σ) and random (σ) components for setup and organ motion derived from analysis of the sample of considered patients

	Σ_{Setup} (mm)	Σ_{Setup} (mm)	$\Sigma_{Organ\ M.}$ (mm)	$\sigma_{Organ\ M.}$ (mm)	Margin (mm)
LL	2.40	3.00	1.35	1.13	7
AP	2.08	2.07	1.92	2.68	9
CC	1.70	1.79	2.25	3.63	9

LL, lateral-lateral; *AP*, anterior-posterior; *CC*, cranial-caudal; *M.*, movement

Organ tracking through fiducial markers and electronic portal imaging is able to reduce the spread of displacements, significantly contributing to improve the ballistic precision of radiation delivery.

IGRT TECHNOLOGIES – CONE BEAM

Radiotherapy and Oncology 121 (2016) 103–108

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

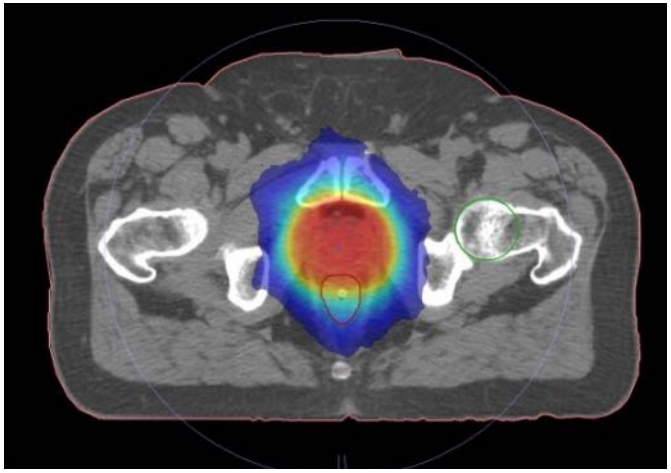
Prostatic cancer IGRT

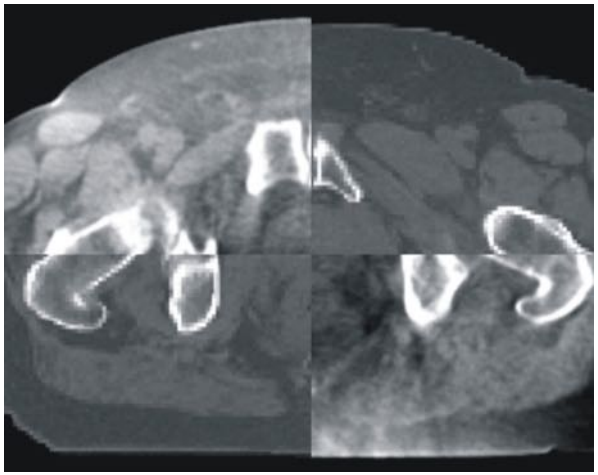
Image-guided radiotherapy for prostate cancer with cone beam CT: dosimetric effects of imaging frequency and PTV margin

Hemal Ariyaratne [a,*], Hayley Chesham [b], John Pettingell [c], Roberto Alonzi [a]

[a] Mount Vernon Cancer Centre, United Kingdom; [b] Radiation Oncology Centres Maroochydore, Australia; [c] Proton Partners International, Newport, United Kingdom

CBCT: visualization of tumor position before each fraction, allowing on-line repositioning and daily assesment of changes in tumour volume and patient's anatomy



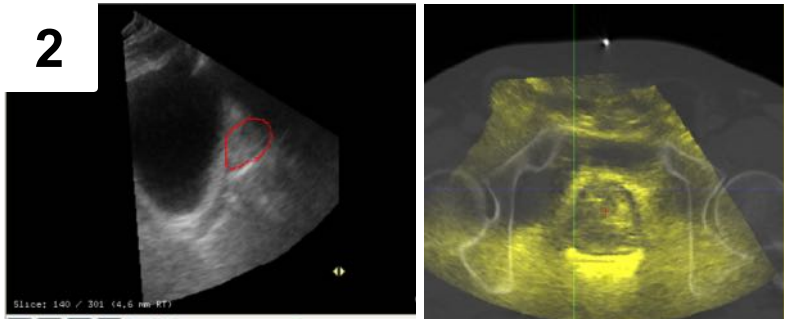


US-CLARITY

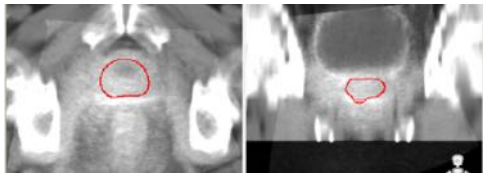
1

3D US localization of the prostate

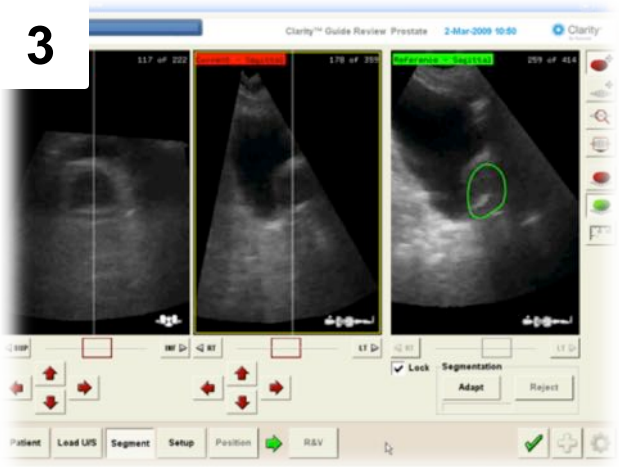
2



PRV (Positioning Reference Volume) definition

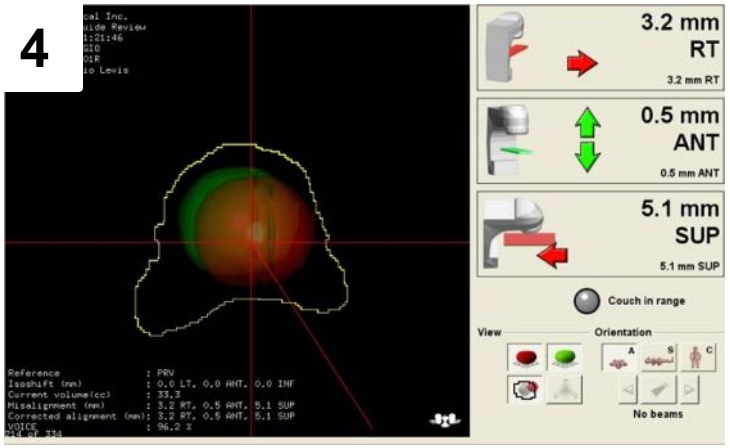


3



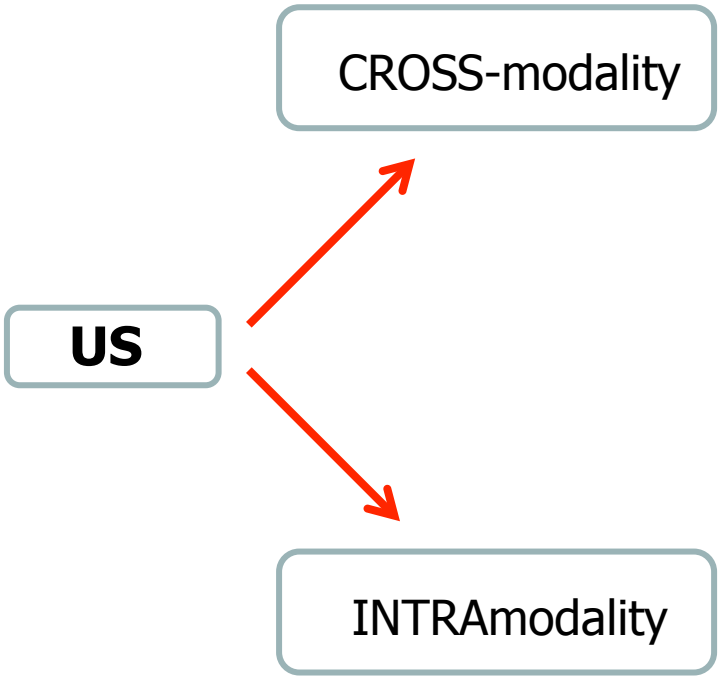
3D US localization of the prostate
Manual segmentation

4



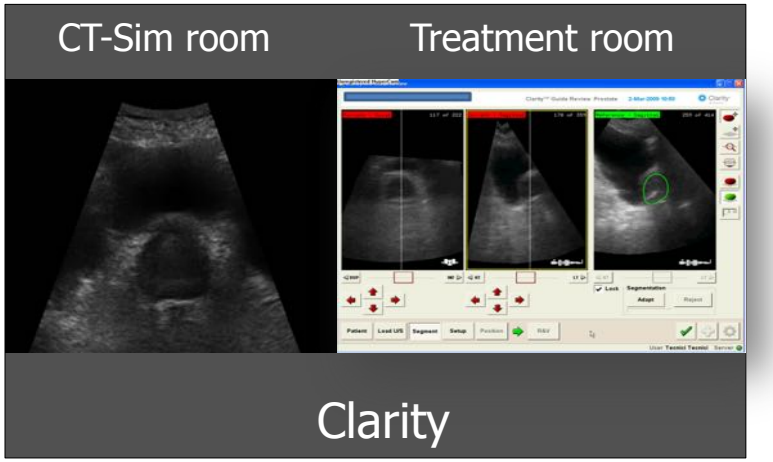
Repositioning based on comparison of planning 3D-US study to daily 3D-US evaluation

CROSS-MODALITY vs INTRAMODALITY



BAT

Sonarray



A more accurate prostate alignment appears to be obtained with IM method

US-CLARITY

JOURNAL OF APPLIED CLINICAL MEDICAL PHYSICS, VOLUME 15, NUMBER 4, 2014

Impact of the observers' experience on daily prostate localization accuracy in ultrasound-based IGRT with the Clarity platform

Christian Fiandra,[1a] Alessia Guarneri,[2] Fernando Muñoz,[2] Francesco Moretto,[1] Andrea Riccardo Filippi,[1] Mario Levis,[1] Riccardo Ragona,[1] and Umberto Ricardi[1]

A training period is recommended in order to learn both the imaging and repositioning procedures

ORIGINAL ARTICLE

Three-Dimensional Ultrasound-Based Image-Guided Hypofractionated Radiotherapy for Intermediate-Risk Prostate Cancer: Results of a Consecutive Case Series

Pierfrancesco Franco[a*], Fernando Munoz[b], Mario Levis[a], Christian Fiandra[a], Alessia Guarneri[b], Francesco Moretto[b], Sara Bartoncini[a], Francesca Arcadipane[a], Serena Badellino[a], Cristina Piva[a], Elisabetta Trino[a], Andrea Ruggieri[a], Andrea Riccardo Filippi[a] & Riccardo Ragona[a]

Cancer Investigation, 2015

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CLARITY PLATFORM PROCEDURE

Patient selection → CT-US co-registration →

Positioning Reference Volume (PRV) definition

Transfer data to LINAC

Patient positioning

- US acquisition
- US images segmentation
- PRV fusion with actual prostate volume
- Registration and couch moving

Treatment delivery

Mean duration time of 3.09 minutes (SD±1.32)

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US: PROs AND CONs BALANCE

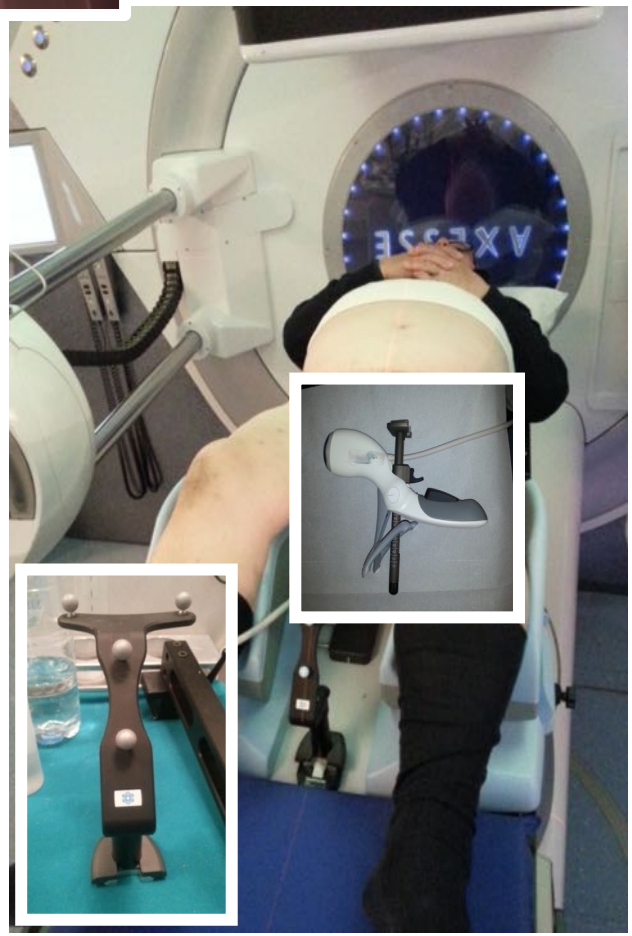
PROs

- FAST
- NON INVASIVE
- EXCELLENT VISUALIZATION OF SOFT TISSUES STRUCTURES
- NON IONIZING METHODS
- COST EFFECTIVE
- NO OVERSTIMATES VOLUME

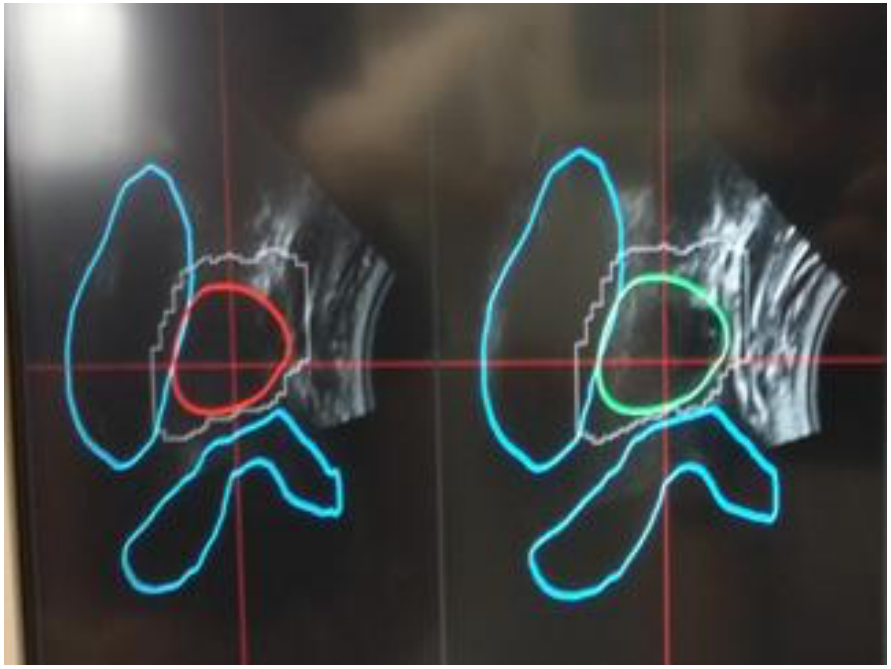
CONs

- OBESITY
- LEARNING CURVE
- BLADDER FILLING COMPLIANCE
- INTER USER VARIATION
- PROBE INDUCED PRESSION?

INTRAFRACTIONAL IMAGING: US-AUTOSCAN

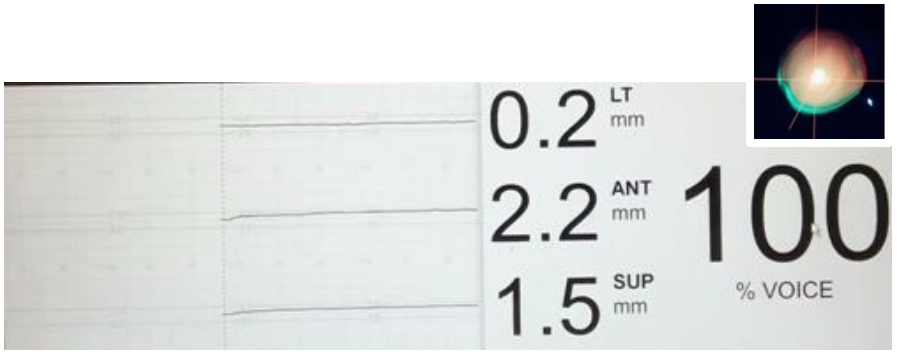


US-AUTOSCAN



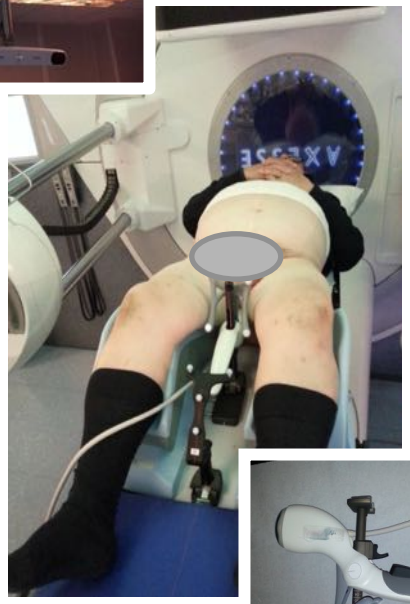
Inter-fraction

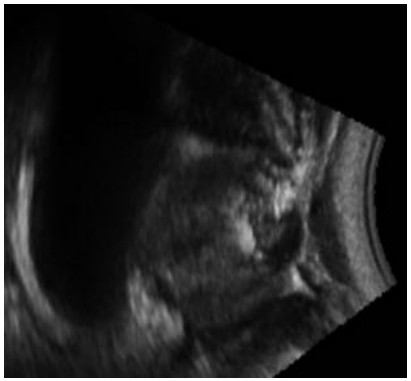
Intra-fraction

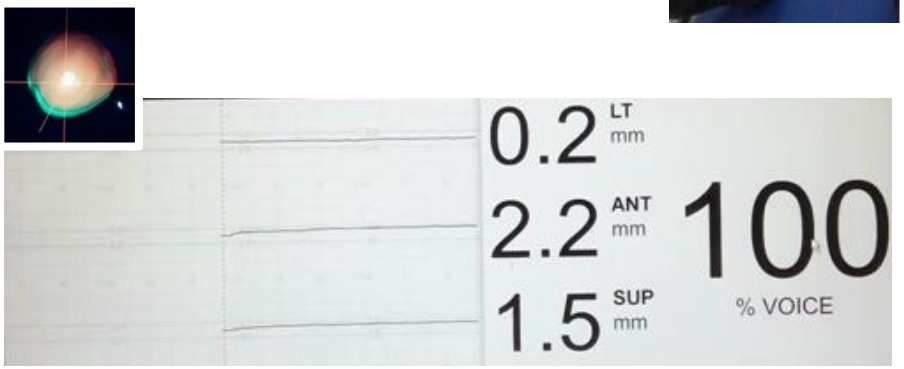


US - AUTOSCAN

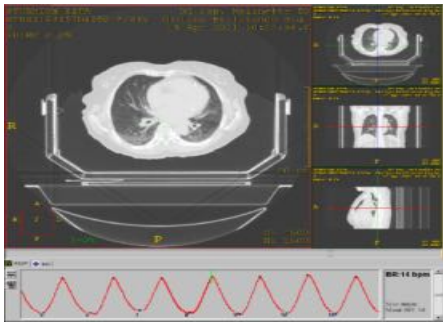
- New system based on acquisitions with a **transperineal ultrasound probe** and an intramodality registration
- Probe with an internal **automed sweeping**
- Monitoring **intrafraction** motions



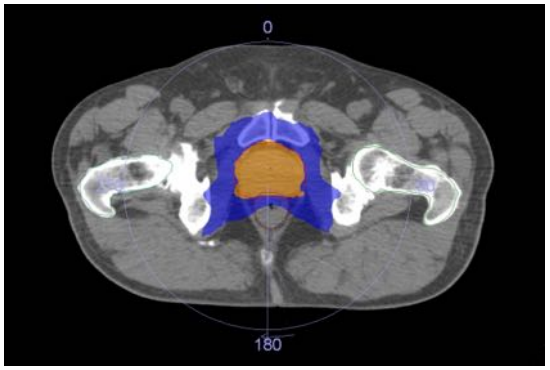




RADIATION TREATMENT

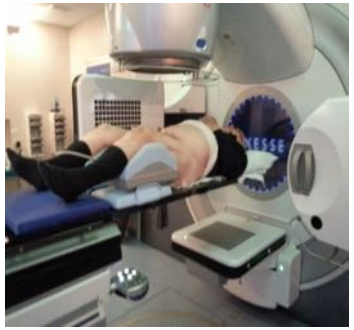


CT or 4D-CT



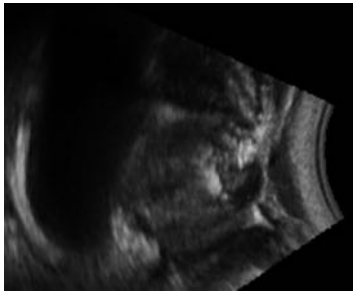
TREATMENT PLAN

Daily CBCT

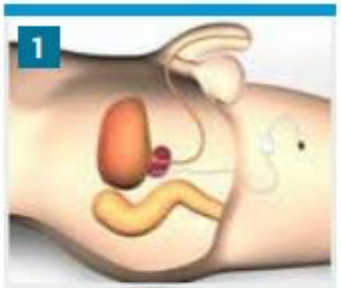


IGRT

DAILY US
Clarity platform with
Autoscan probe



RAYPILOT SYSTEM



PRE-TREATMENT

Insert the RayPilot® transmitter in the ROI to track before the CT and dose planning.

DURING TREATMENT

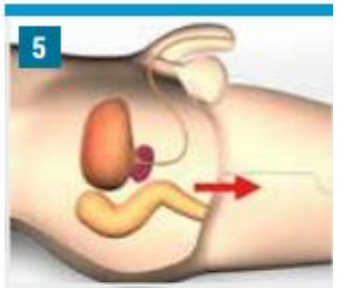
Position the RayPilot® receiving system on the treatment couch, place the patient in treatment position and connect the RayPilot® transmitter.

DURING TREATMENT

The RayPilot® transmitter sends out a positioning signal to the RayPilot® receiving system. Move the treatment table according to the instructions in order to put the ROI into the desired position.

DURING TREATMENT

The RayPilot® system tracks and record the ROI continuously during the radiotherapy session. A warning occurs if the ROI moves out of the predefined margin.



POST-TREATMENT

Remove the RayPilot® transmitter after the final treatment.

No foreign objects are left in the body.

BENEFITS

- Objective and fast patient set up without X-ray
- Automatic patient identification
- Real time target positioning
- In situ dosimetry
- Time stamped positioning data
- Follow up and treatment analyses

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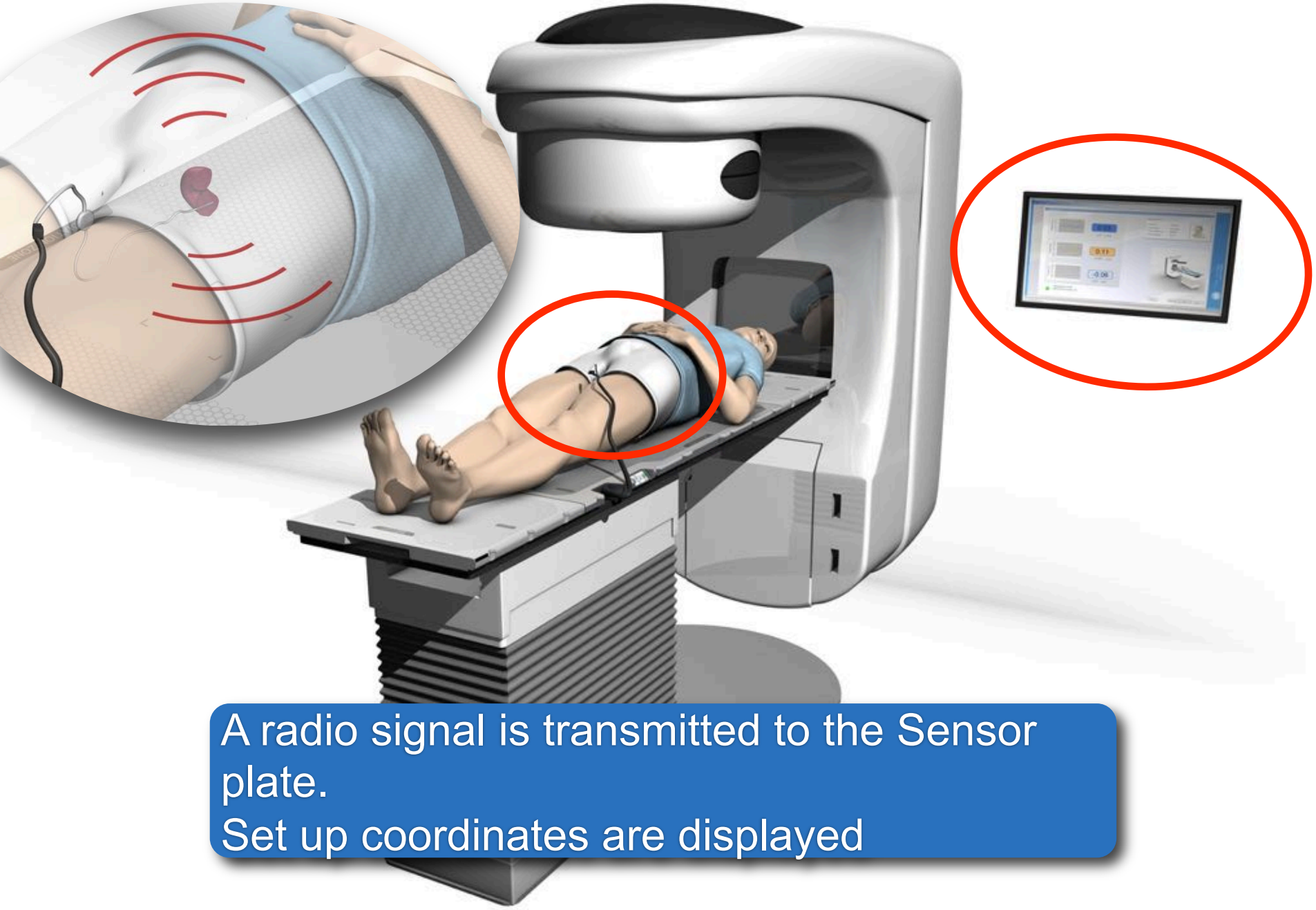
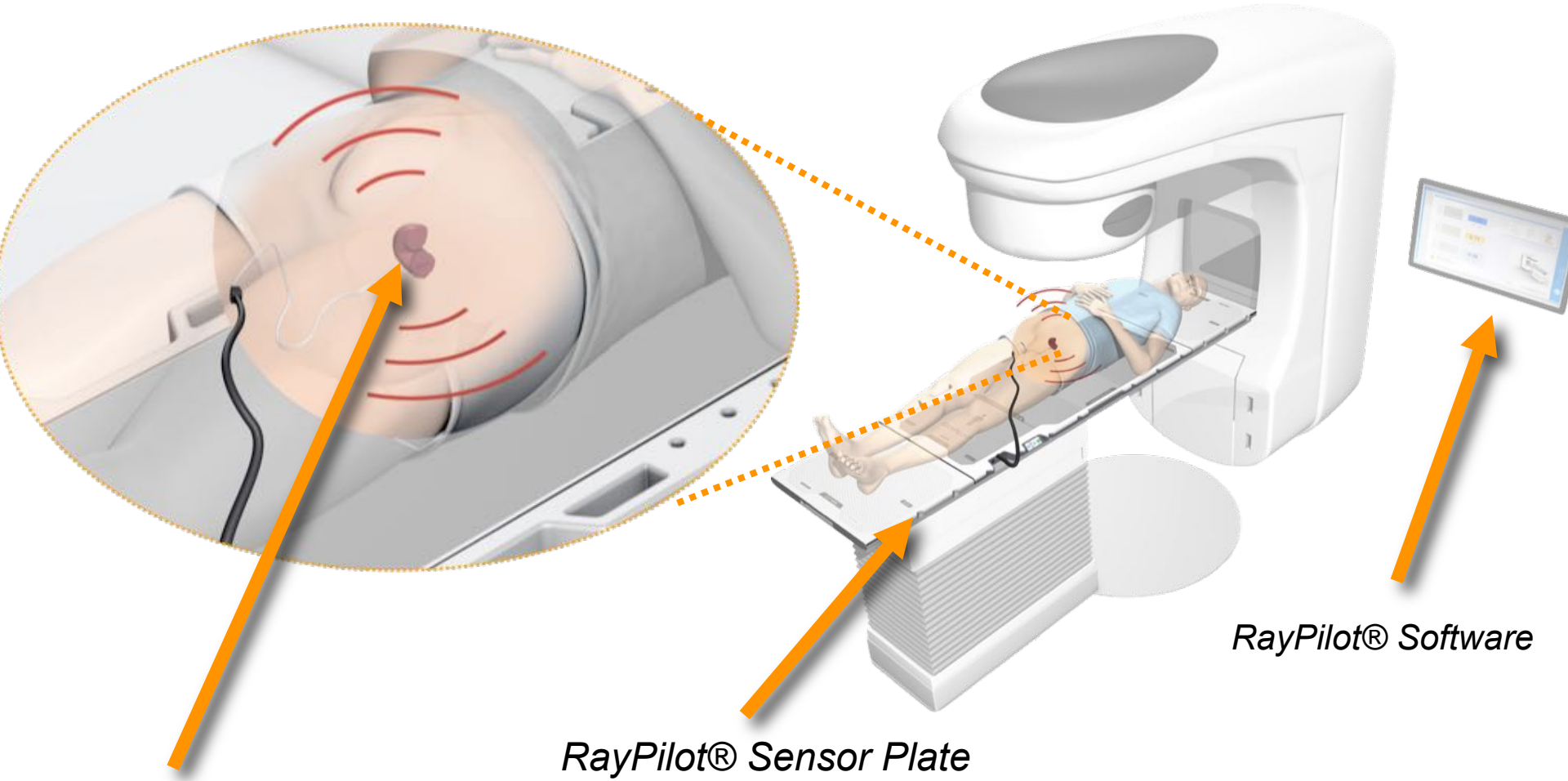

A radio signal is transmitted to the Sensor plate.
Set up coordinates are displayed

The main parts of the RayPilot® system

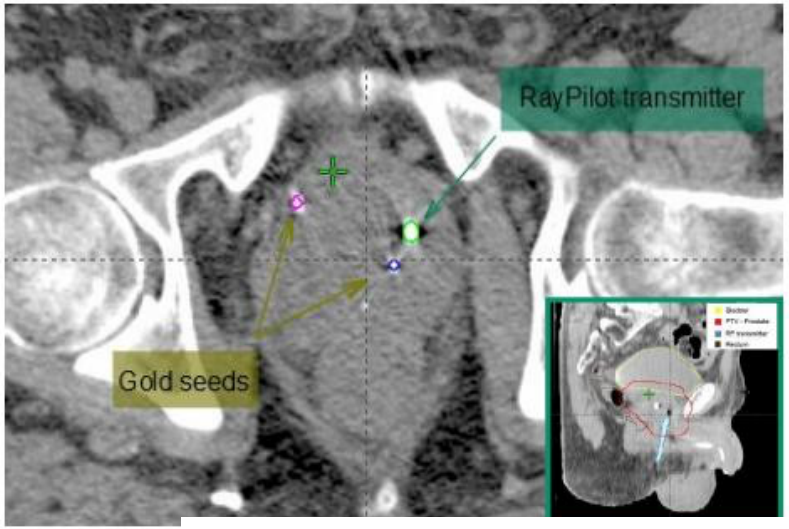


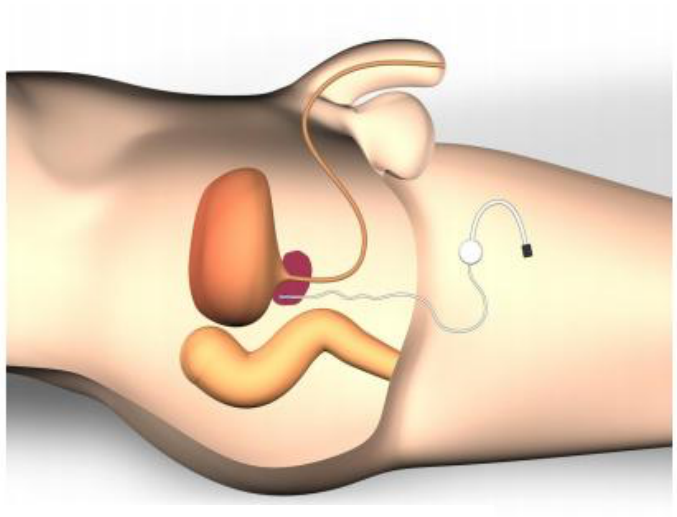
RayPilot® Transmitter

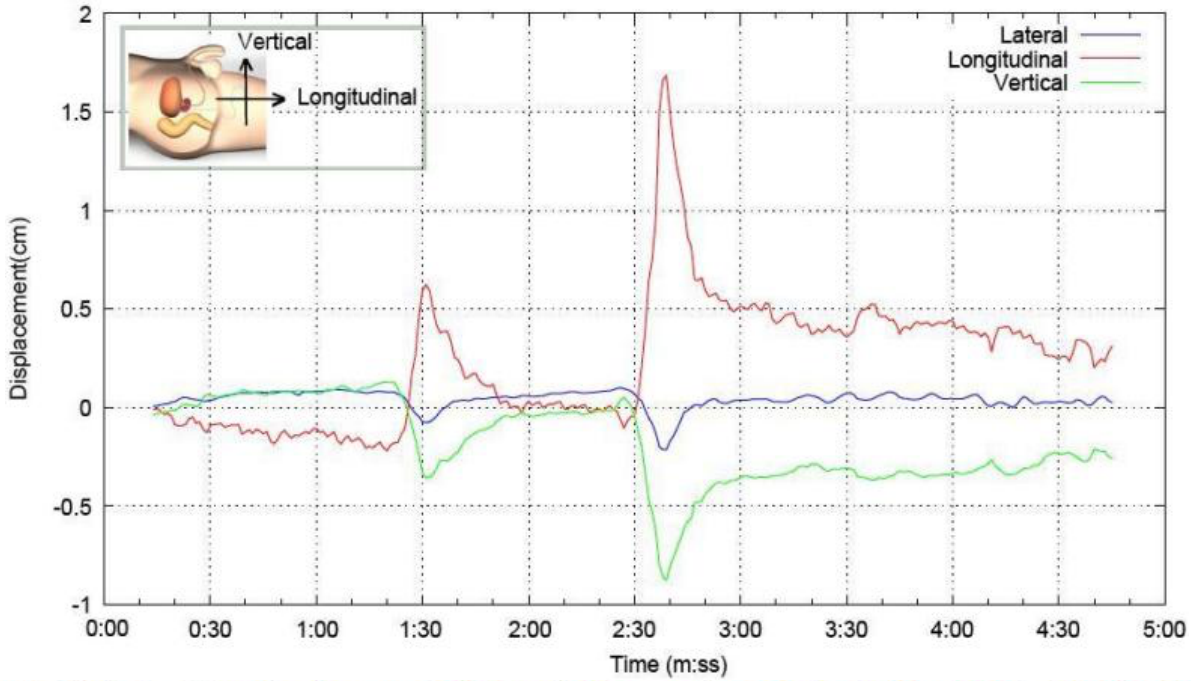
RayPilot® Sensor Plate

RayPilot® Software

RAYPILOT







Recorded intrafraction displacement. A transient excursion of about 20 seconds duration is shown.

UNIVERSITY OF TURIN

Between January 2010 and June 2017

325 intermediate prostate cancer patients underwent **hypofractionated RT** using daily IGRT

- **IGRT:** CBCT or 3D-US imaging (Clarity™)
- Daily on-line **target localization** prior RT
- In selected case, **hormonal therapy** for 6 months

STUDY INCLUSION CRITERIA

a) **intermediate risk-group**
b) pretreatment staging (PSA, DRE)
c) prostate biopsy
d) histologically confirmed prostate adenocarcinoma
e) International Prostatic Symptoms Score (IPSS) < 12

STUDY EXCLUSION CRITERIA

a) low compliance to treatment protocol (no adequate bladder filling, rectal volume >100 cc)
b) obese patients and/or other conditions limiting US visualization of the prostate gland
c) previous abdominal surgery

HYPOFRACTIONATED RADIATION SCHEDULE

SIB

70,2 Gy/26 fr to prostate (2,7 Gy/day)

61,1 Gy to prostate+SV (2,35 Gy/day)

BED_2 = 84,4 Gy if α/β = 1,5 Gy 80 Gy if α/β = 3 Gy

TARGET VOLUME DEFINITION

PTV (Elekta Precise™) **:** CTV + 10 mm in all directions and 7 mm posteriorly

PTV (Elekta Axesse™): CTV + 7 mm in all directions and 5 mm posteriorly

TREATMENT PLANNING

3DCRT or IMRT (7 static fields step&shoot / VMAT single arc)

CONSTRAINTS

Rectum (V_{67}<15% o V_{58}<25%)

Bladder (V_{64}<35% o V_{73}<15% o V_{70}<25%)

Femoral heads (D_{mean} <44.4 Gy)

UNIVERSITY OF TURIN – CLINICAL OUTCOMES

Caratteristiche pazienti		N (%)
ETA'		
	< 70 anni	81 (24.9)
	≥ 70 anni	244 (75.1)
	Media	73
	Range	53.5-82.6
z-PSA		
	<10 ng/ml	207 (63.7)
	10-19.9 ng/ml	118 (36.3)
GS		
	3+3	75 (23.1)
	3+4	138 (42.5)
	4+3	84 (25.8)
STADIO		
	cT1c	197 (60,6)
	cT2a	10 (3.1)
	cT2b	15 (4.6)
	cT2c	93 (28.6)
TURP		
	Si	23 (7.3)
	No	302 (92.7)
OT		
	Si	120 (36.9)
	No	205 (63.1)

Treatment charateristic		N (%)
TECNIQUE	3DCRT	44 (13.5)
	IMRT	152 (46.8)
	VMAT	129 (39.7)
IGRT	ULTRASOUND	243 (74.7)
	CBCT	82 (25.3)

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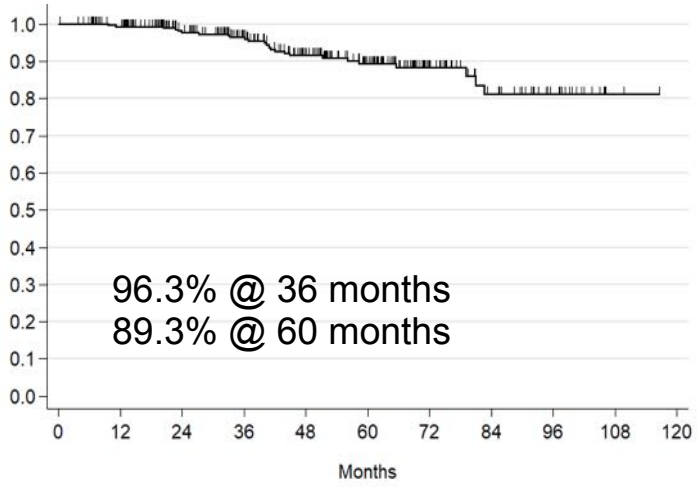
UNIVERSITY OF TURIN – CLINICAL OUTCOMES

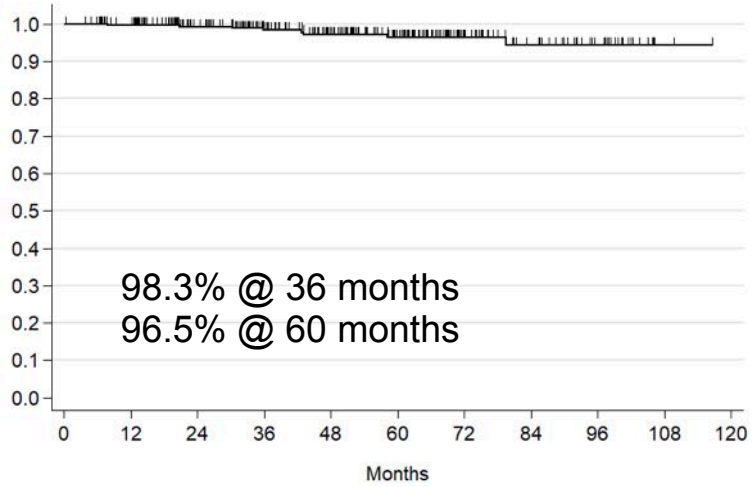
- Median follow-up: **52,3 months** (range 6 – 106 months)
- Biochemical relapse free survival: **89.3% at 60 months**
- Median time to biochemical failure: 45.5 months (range 11.6 - 96.7 months)
- 25 patients experienced **biochemical failure** (11 loco-regional and 9 distant failure)
- **13 death:** only 3 patients died from disease, while other 10 died from other causes

UNIVERSITY OF TURIN – CLINICAL OUTCOMES

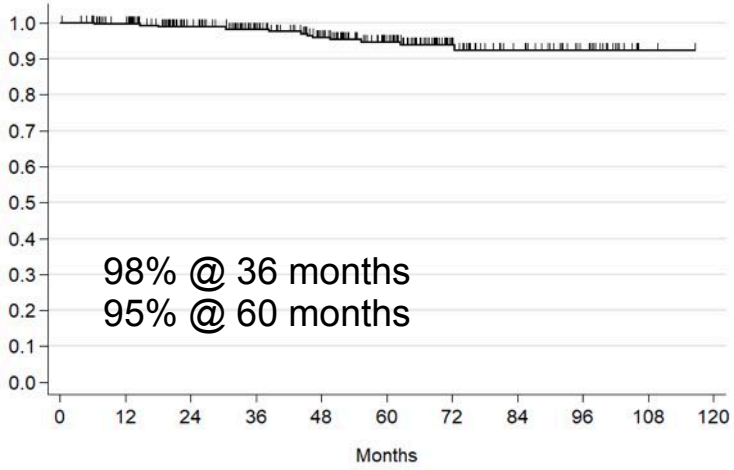
Biochemical disease free survival



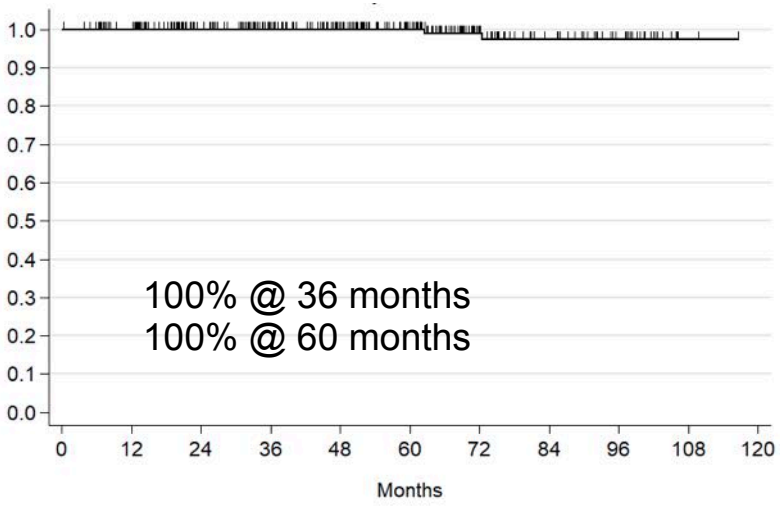
Disease free survival



Overall Survival

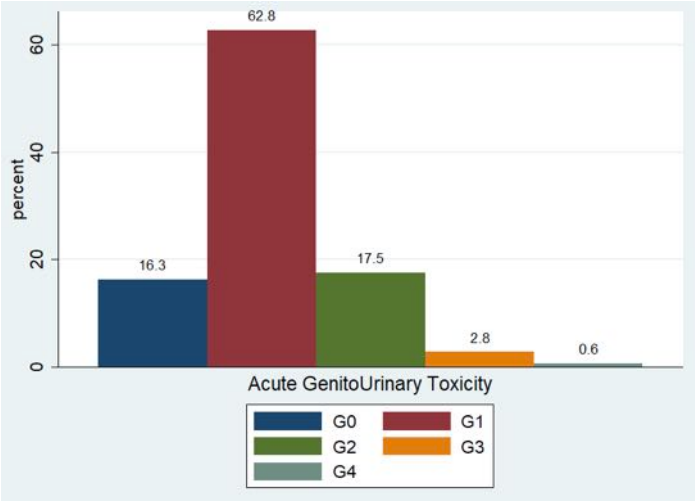


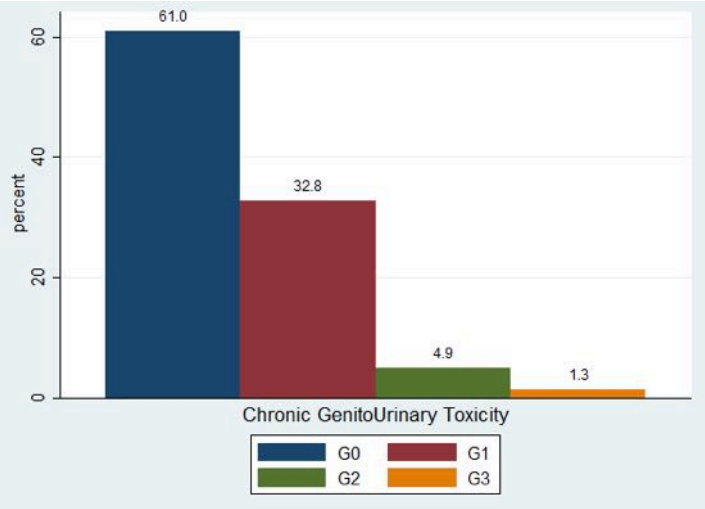
Cancer Specific Survival



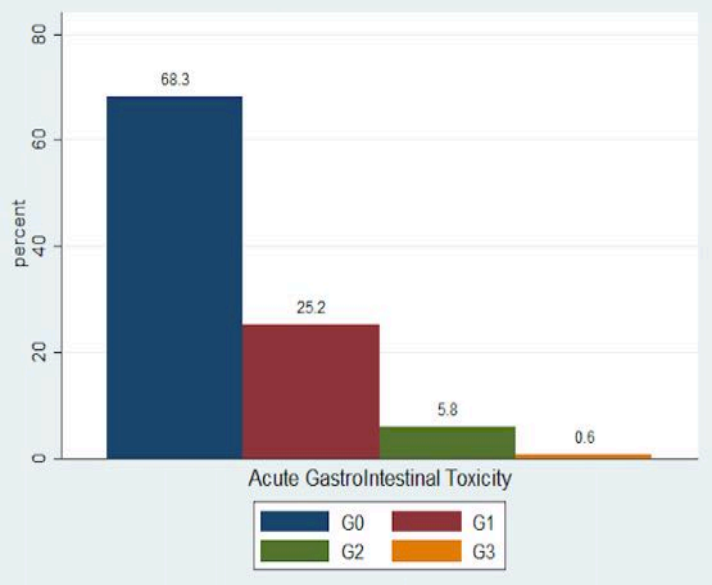
UNIVERSITY OF TURIN – CLINICAL OUTCOMES

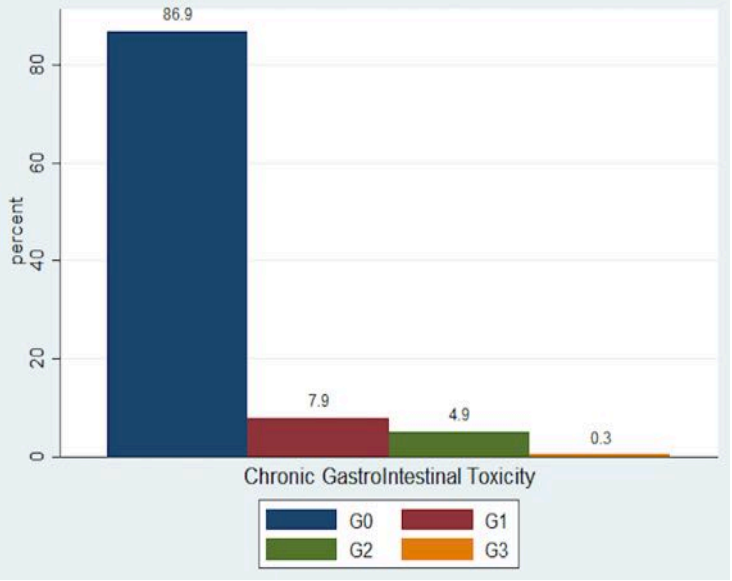
Toxicity GU





Toxicity GI





ANCILLARY STUDY – IGRT METHODS COMPARISON

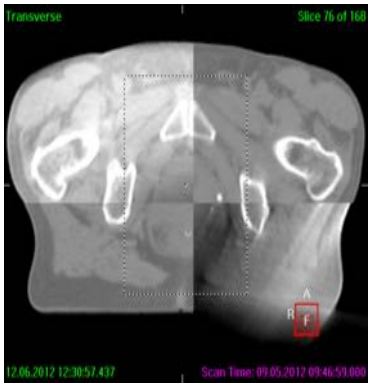
Between April 2015 and July 2016

intermediate prostate cancer patients underwent hypofractionated RT using daily IGRT

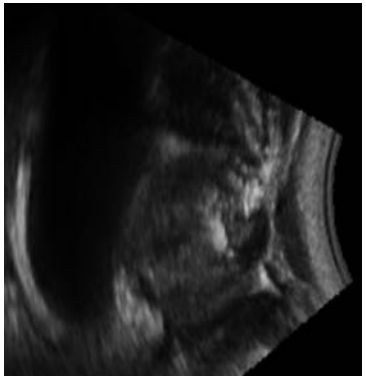
Good prostate gland visualization with **both Clarity and Autoscan system**

3 groups of IGRT modality comparison

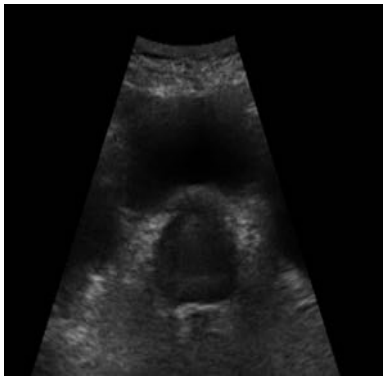
CLARITY vs CBCT



AUTOSCAN vs CBCT



CLARITY vs AUTOSCAN



Patient repositioning always based on Clarity or CBCT results

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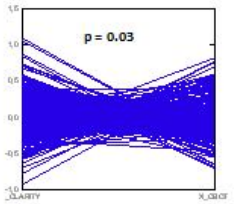
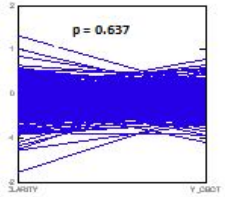
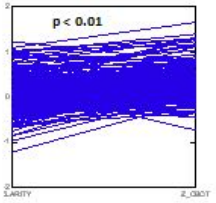
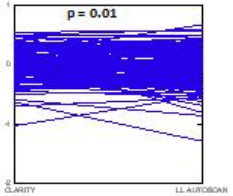
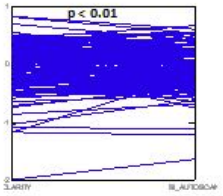
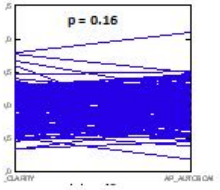
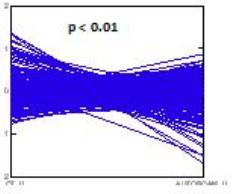
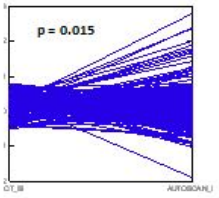
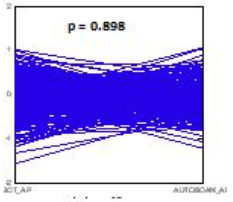
RESULTS – IGRT METHODS COMPARISON

	LL	SI	AP
Clarity Vs. CBCT			
Clarity Vs. Autoscan			
Autoscan Vs. CBCT			

13 patients: 269 data

9 patients: 234 data

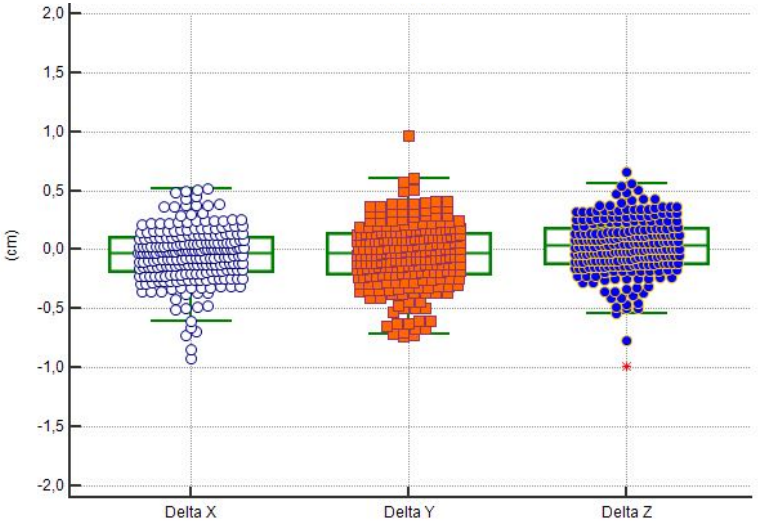
11 patients: 268 data

	LL	SI	AP
Clarity - CBCT	37	34	5
Clarity - Autoscan	0	10	5
Autoscan - CBCT	21	23	25

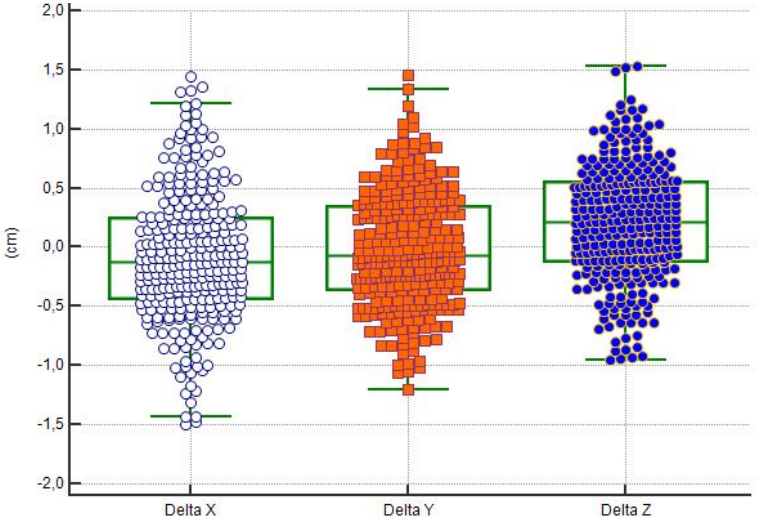
RESULTS – IGRT METHODS COMPARISON

	LL	SI	AP
Clarity - CBCT	0.076 ± 0.564	-0.014 ± 0.496	0,246 ± 0,483
Clarity - Autoscan	-0,05 ± 0,246	-0,068 ± 0,29	0,028 ± 0,254
Autoscan - CBCT	-0,141 ± 0,698	-0,102 ± 0,688	0,005 ± 0,587

Autoscan



CBCT



US - AUTOSCAN

Contents lists available at ScienceDirect

Radiography

journal homepage: www.elsevier.com/locate/radi

Intrafraction monitoring of prostate motion during radiotherapy using the Clarity® Autoscan Transperineal Ultrasound (TPUS) system

A.K. Richardson*, P. Jacobs

Bristol Haematology and Oncology Centre, Horfield Road, Bristol, BS2 8ED, UK

- Displacements 52%, 8% and 2% at 3, 7 and 10 mm thresholds respectively
- Posterior motion was most common

CONCLUSION

- Hypofractionated treatment: **well-tolerated and effective** treatment option
- **Clarity 3D-US** based IGRT is used into daily clinical practice as **reference IGRT modality** with reliable clinical results in terms of efficacy and toxicity
- **US-Autoscan** seems to be an accurate IGRT method
- US-Autoscan: fast and reliable method to ensure **accurate delivery** of treatment plans
- **Further investigations** are necessary for evaluating the performances of intrafraction monitoring with this device

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CONCLUSION

Whatever modality you choose to treat the prostate:

The proper treatment requires a system of IGRT that allows very accurate localization

No matter how good is the beam, if the target is not where we thought

Grazie!

Keith Haring
- Wallpaper