

IMAGING IN SBRT E ASPETTI TECNICO/DOSIMETRICI CORRELATI



Stefania Clemente
SSD Fisica Sanitaria
IRCCS CROB Rionero in Vulture (PZ)



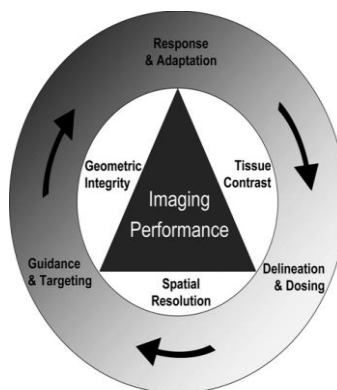
UNIVERSITÀ DEGLI STUDI
DI MILANO

Stereotactic Body
Radiation Therapy

Università di Milano
24/25 ottobre 2014

G.d.L.
SBRT

Imaging
accuracy in
SBRT for
Target
Volume (TV)
and OARs
determinati
on



Dawson & Ménard. The Oncologist
2010

G.d.L. SBRT AIFM
S.Clemente

Multimodality imaging for TVD in SBRT



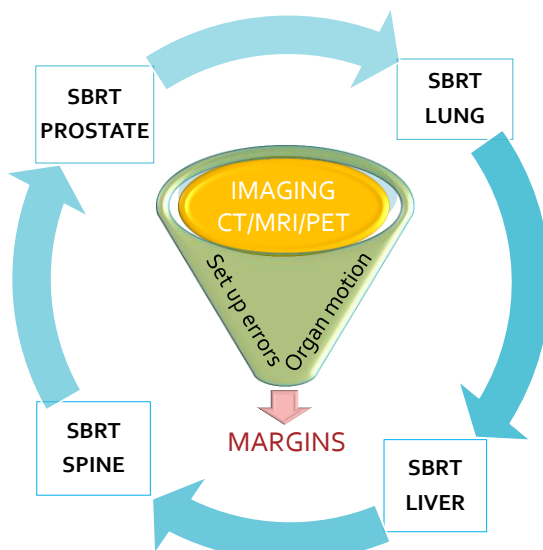
Patel et al. Radiation Research 2012

Modality	Uses	Limitations
CT	High depth penetration. High spatial resolution. Whole body anatomical imaging.	Ionizing radiation exposure. Expensive. Low spatial resolution.
MRI	High depth penetration. High spatial resolution. Whole body anatomical imaging.	Ionizing radiation. Expensive. Low spatial resolution.
Positron emission tomography.	High depth penetration. Whole body molecular imaging. Quantitative sensitivity. High sensitivity. High depth penetration.	Expensive. Long acquisition time. Expensive.
Positron emission computed tomography.	Whole body molecular imaging.	Long acquisition time. Expensive.

Nanoparticles	Imaging Modality	In vivo Applications
Liposomes	Gamma imaging, SPECT, PET	Clinically utilized to target tumor cells in breast, brain, head and neck, lung, and lymphoma
Iron oxide (Paramagnetic nanoparticles)	MRI, PET/CT, MR/PET	Image tumor angiogenesis. Single and multimodal imaging.
Quantum dots	PET, optical imaging	Image tumor angiogenesis. Single and multimodal imaging. Study tumor microenvironment.
Dendrimers	MRI, CT, optical imaging, PET, SPECT	Image tumor angiogenesis. Single and multimodal imaging. Study tumor microenvironment.
Gold	SERS	Tumor imaging.

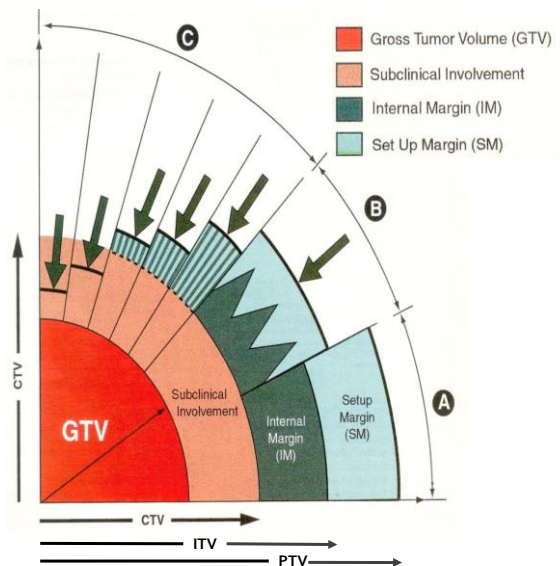
G.d.L. SBRT AIFM
S.Clemente

From imaging to margins



G.d.L. SBRT AIFM
S.Clemente

From imaging to margins in SBRT (ICRU 50-62)



G.d.L. SBRT AIFM
S.Clemente

Setup- errors manageme nt in SBRT



Motion Management: Q-fix



Pro-Lok Civco



CDR System



Body- fix



G.d.L. SBRT AIFM
S.Clemente

4088 Benedict *et al.*: Stereotactic body radiation therapy: The report of TG101

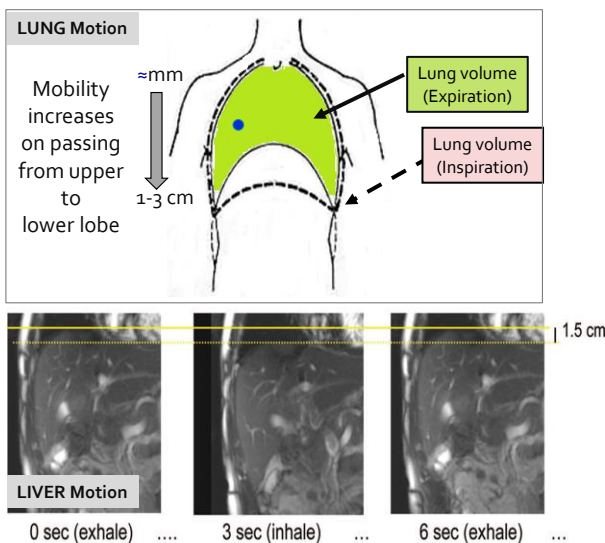
4088

TABLE IV. Achievable accuracies reported in the literature categorized by body site and immobilization/repositioning device.

Author, year	Site	Immobilization/repositioning	Reported accuracy
Lax, 1994 ^a	Abdomen	Wood frame/stereotactic coordinates on box to skin marks	3.7 mm Lat, 5.7 mm Long
Hamilton, 1995 ^b	Spine	Screw fixation of spinous processes to box	2 mm
Murphy, 1997 ^c	Spine	Frameless/implanted fiducial markers with real-time imaging and tracking	1.6 mm radial
Lohr, 1999 ^d	Spine	Body cast with stereotactic coordinates	≤3.6 mm mean vector
Yenice, 2003 ^e	Spine	Custom stereotactic frame and in-room CT guidance	1.5 mm system accuracy, 2–3 mm positioning accuracy
Chang, 2004 ^f	Spine	MIT TM BodyFix with stereotactic frame/linac/CT on rails with 6D robotic couch	1 mm system accuracy
Tokuuye, 1997	Liver	Prone position jaw and arm straps	5 mm
Nakagawa, 2000 ^g	Thoracic	MVCT on linac	Not reported
Wulf, 2000 ^h	Lung, liver	Elekta TM body frame	3.3mm lat, 4.4 mm long Bony anatomy translation 0.4, 0.1, 1.6 mm (mean X, Y, Z); tumor translation before image guidance 2.9, 2.5, 3.2 mm (mean X, Y, Z)
Fuss, 2004 ⁱ	Lung, liver	MIT TM BodyFix	2.5, 3.2 mm (mean X, Y, Z)
Herfarth, 2001 ^j	Liver	Leibinger body frame	1.8–4.4 mm
Nagata, 2002 ^k	Lung	Elekta TM body frame	2 mm
Fukumoto, 2002 ^l	Lung	Elekta TM body frame	Not reported
Hara, 2002 ^m	Lung	Custom bed transferred to treatment unit after confirmatory scan	2 mm
Hof, 2003 ⁿ	Lung	Leibinger body frame	1.8–4 mm
Timmerman, 2003 ^o	Lung	Elekta TM body frame	Approx. 5 mm
Wang, 2006 ^p	Lung	Medical Intelligence body frame stereotactic coordinates/CT on rails	0.3 ± 1.8 mm AP, -1.8 ± 3.2 mm Lat, 1.5 ± 3.7 mm SI

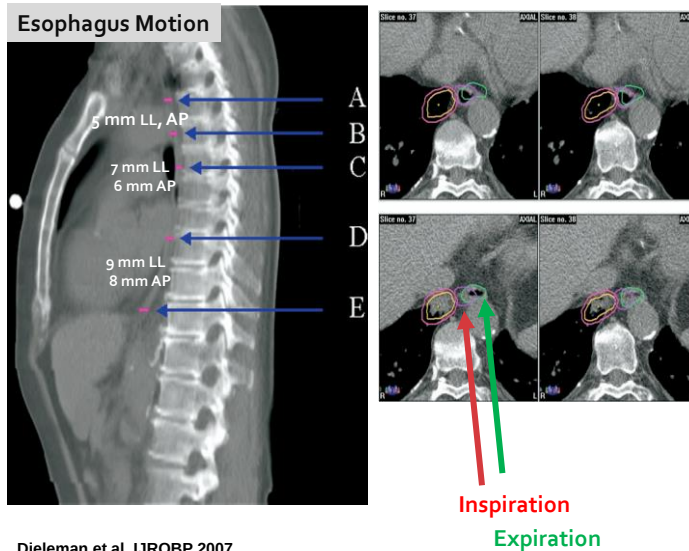
IMAGING IN SBRT
LUNG AND LIVER

Tumor motion management



G.d.L. SBRT AIFM
S.Clemente

Organ motion management



Dieleman et al. IJROBP 2007

G.d.L. SBRT AIFM
S.Clemente

Imaging CT for mobile tumors: artifacts



Discontinuity in the
liver anatomy

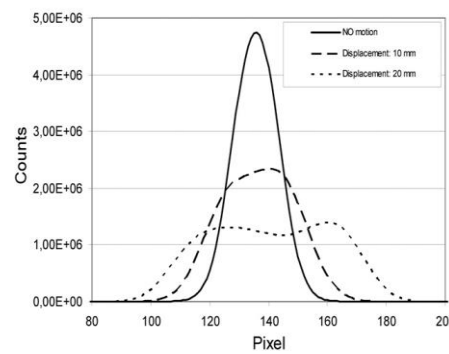
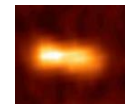


Split of the organ
in two pieces

Bettinardi et al. Seminars in
NM 2012

G.d.L. SBRT AIFM
S.Clemente

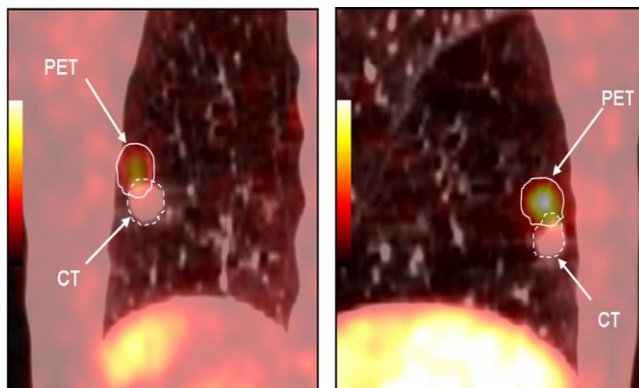
Imaging PET for mobile tumors: artifacts



Optimal activity
threshold:
• motion
• object volume
• source-to-
background

G.d.L. SBRT AIFM
S.Clemente

Imaging PET/CT for mobile tumors: artifacts



Bettinardi et al. Seminars in
NM 2012

G.d.L. SBRT AIFM
S.Clemente

Tumor motion strategies in SBRT (AAPM TG 76)



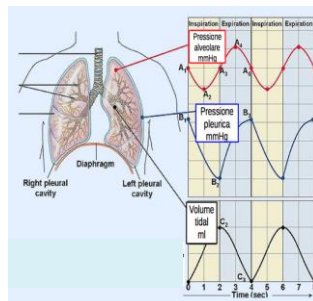
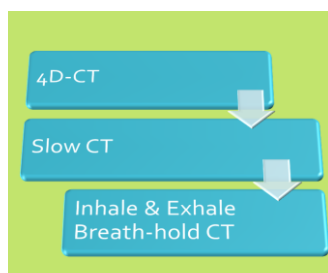
1. **Motion-encompassing**
 - 4D-CT
 - Slow CT
 - Inhale/exhale breath-hold CT
2. **Motion compensating**
 - Respiratory gating
 - Respiration-synchronized (tracking)
3. **Motion restrictive**
 - Breath-hold
 - Forced shallow-breathing with AC

G.d.L. SBRT AIFM
S.Clemente

Tumor motion strategies in SBRT (AAPM TG 76)

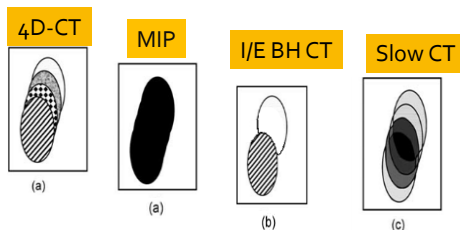
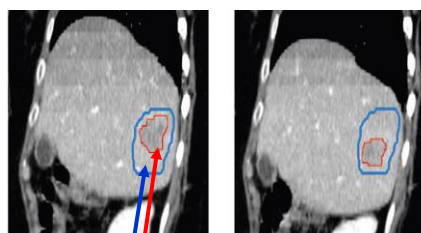


1. Motion- encompassing

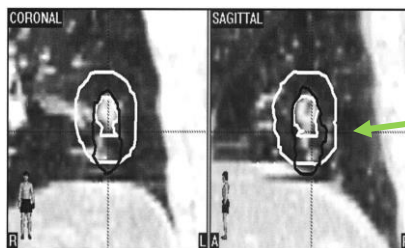


G.d.L. SBRT AIFM
S.Clemente

Motion encompassing strategies for TVD

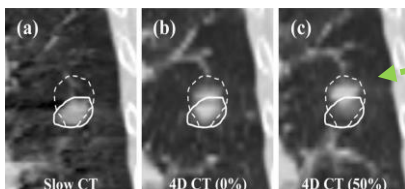


Motion encompassing strategies for TVD



4D-CT vs Fast CT

Underberg et al. R&O 2004

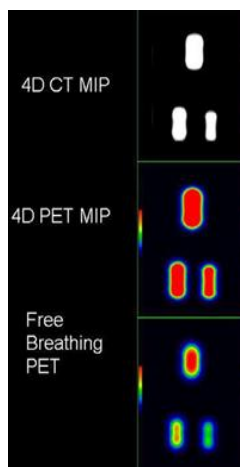


4D-CT vs Slow CT

Nakamura et al. Med. Phys 2008

G.d.L. SBRT AIFM
S.Clemente

Motion encompassing strategies for TVD



4D-PET/CT MIP VOLUMES
CONSISTENT
WITH 4D-CT MIP VOLUMES

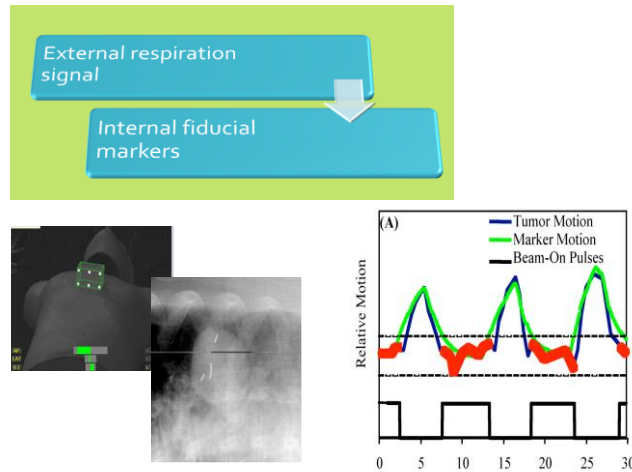
Callahan et al.
IJROBP 2013

G.d.L. SBRT AIFM
S.Clemente

Tumor
motion
strategies
in SBRT:
motion
compensatin
g
(AAPM TG
76)



2. Respiratory gating methods

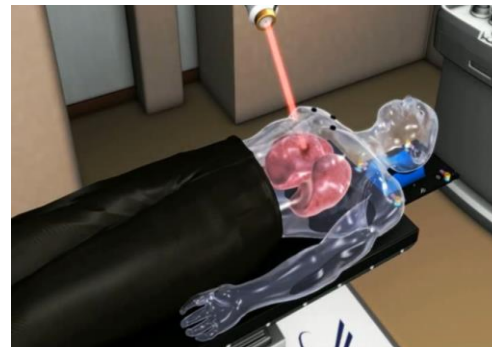


G.d.L. SBRT AIFM
S.Clemente

Tumor
motion
strategies
in SBRT:
motion
compensatin
g
(AAPM TG
76)



2. Respiratory tracking methods



G.d.L. SBRT AIFM
S.Clemente

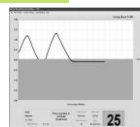
Tumor
motion
strategies
in SBRT:
motion
restrictive
(AAPM TG
76)



3. Breath-hold methods



To maximize organ
stability,
reproducibility and
comfort
for the patient

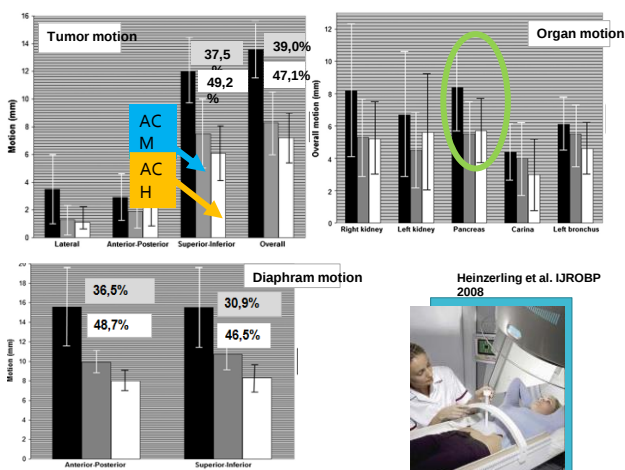


G.d.L. SBRT AIFM
S.Clemente

Tumor
motion
strategies
in SBRT:
motion
restrictive
(AAPM TG
76)



3. Forced shallow breathing with AC

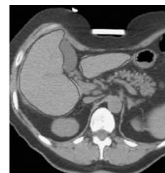


G.d.L. SBRT AIFM
S.Clemente

Tumor motion strategies in SBRT: motion restrictive (AAPM TG 76)



Liver deformations in patients undergoing SBRT under AC were small ($< 5\text{mm}$)

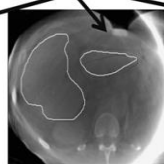


Planning CT

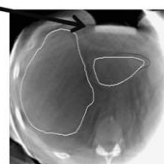
Abdominal compression plate



CBCT
1



CBCT
5



CBCT
6

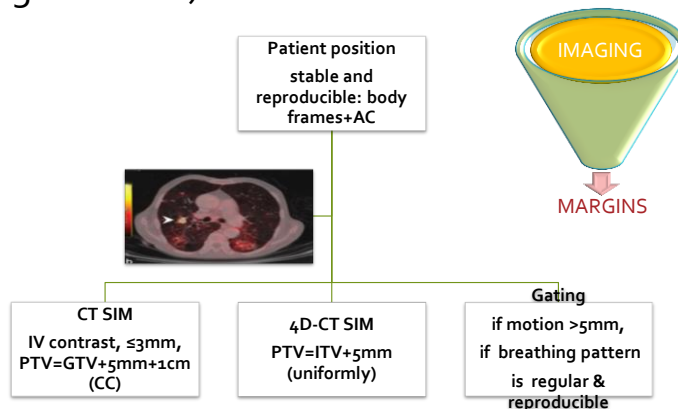
Eccles et al. IJROBP
2010

G.d.L. SBRT AIFM
S.Clemente

Imaging protocol for TVD in SBRT Lung



LUNG (RTOG 813 and 915-EORTC as guidelines)

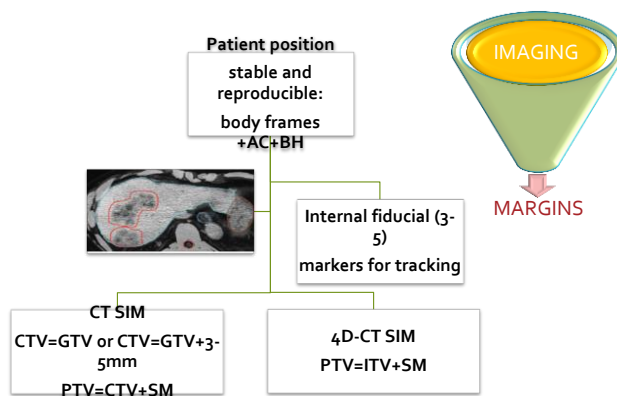


G.d.L. SBRT AIFM
S.Clemente

Imaging protocol for TVD in SBRT Liver



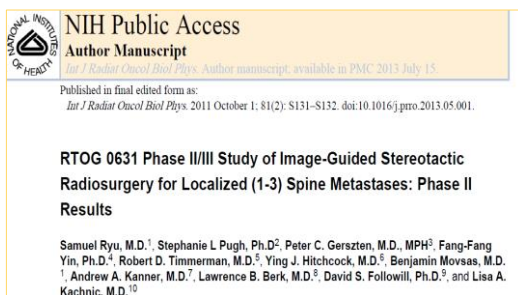
LIVER (RTOG 438 as guidelines)



G.d.L. SBRT AIFM
S.Clemente

IMAGING IN SBRT SPINE

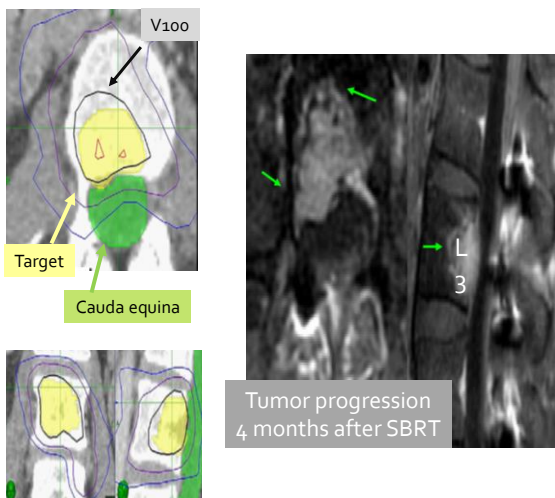
Imaging SBRT Spine



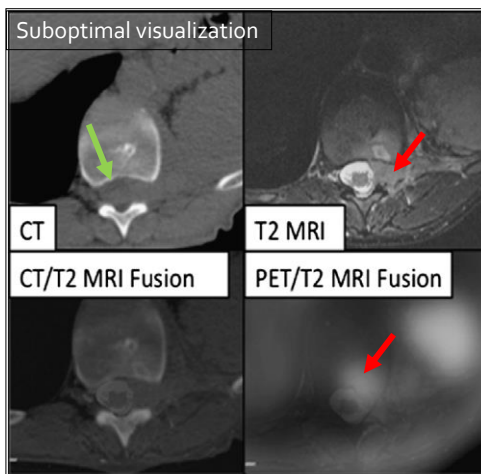
Single fraction dose of 16 Gy

Feasibility and accurate use of SRS to treat spinal metastases, with rigorous quality control

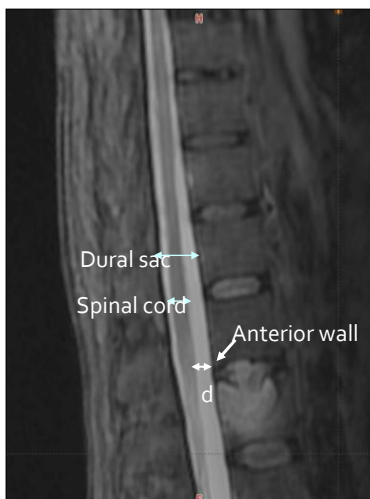
Imaging for TVD in SBRT Spine



Imaging for TVD in SBRT Spine



Imaging for TVD in SBRT Spine



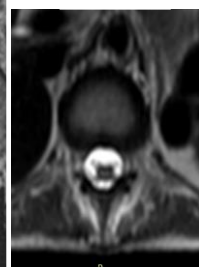
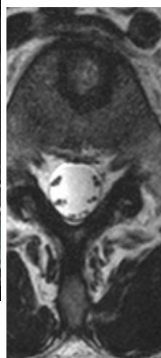
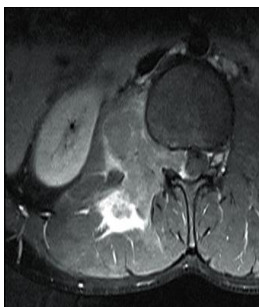
Variable location (d) of
the spinal cord/cauda
equina relative to the
anterior wall of the
spinal canal

Imaging MRI 3T for TVD in SBRT Spine



MR IMAGING OF THE SPINE AT HIGH FIELD

Table 1. Solutions for 3D FSE MRI			
Problems	Old solutions	New problems	New solutions
Long acquisition time	Decreased TR	Decreased CSF signal	Driven equilibrium pulse
	Increase ETL or TF	Increase blurring	SPACE readout
CSF pulsation artifact	Decreased no. of phase-encoded steps	Decreased spatial resolution	Parallel imaging



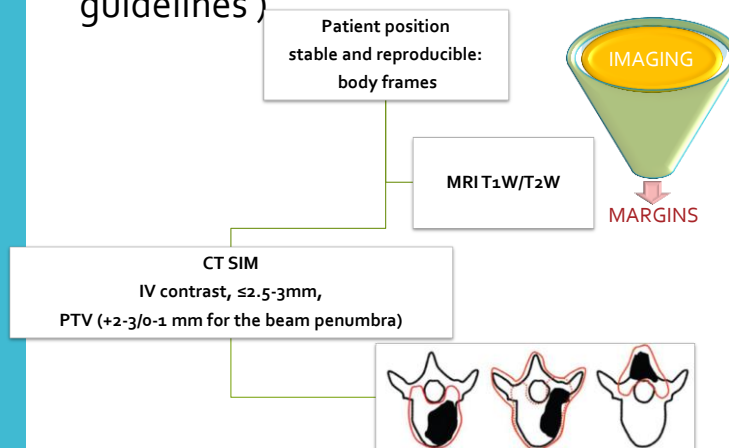
G.d.L.
SBRT

G.d.L. SBRT AIFM
S.Clemente

Imaging protocol for TVD in SBRT Spine



SPINE cases (RTOG 613 as guidelines)



G.d.L. SBRT AIFM
S.Clemente

IMAGING IN SBRT PROSTATE

Imaging for TVD in SBRT Prostate



CT scans overestimate prostate volume by 35% vs MRI

Base	CT (cm ²)	MRT (cm ²)	DISCREPANCY (cm ²)
MRI defined Base of prostate	17.3 ± 4.6	10.9 ± 3.4	6.4 ± 3.6
region of NVB	19.6 ± 4.6	14.3 ± 3.8	5.3 ± 2.3
5 mm superior to CT center	19.2 ± 4.5	14.0 ± 3.9	5.2 ± 2.0
X CT center	18.2 ± 4.4	13.2 ± 3.8	5.0 ± 1.9
5 mm inferior to CT center	16.4 ± 4.1	11.2 ± 3.7	5.2 ± 2.0
MRI defined Apex	11.51 ± 2.3	5.5 ± 1.7	6.0 ± 2.6
Apex			

Hentschel et al. Strahlenther Onkol 2011

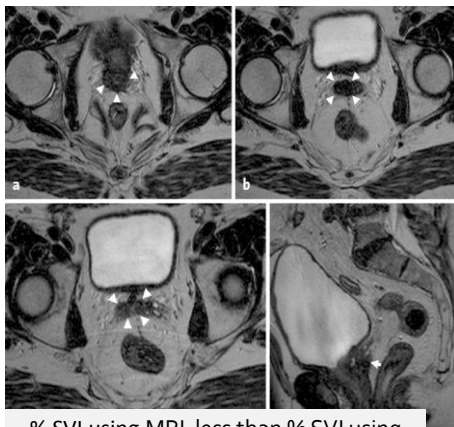
G.d.L. SBRT AIFM
S.Clemente

Imaging for TVD in SBRT Prostate



SVI identified by MRI

entschel et al. StrahlentherOnkol 2011

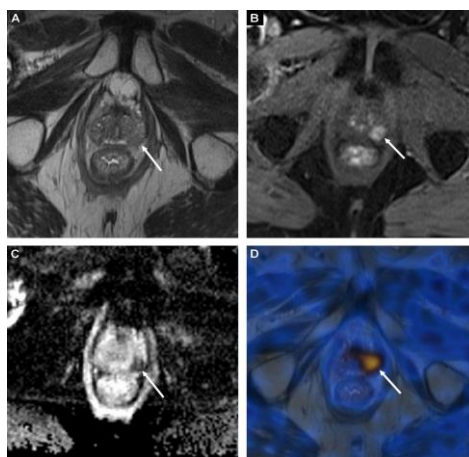


% SVI using MRI less than % SVI using
Roach-Díaz

$$\text{SVI} = \text{PSA value} + (\text{Gleason score} - 6) \times 10$$

G.d.L. SBRT AIFM
S.Clemente

Imaging for TVD in SBRT Prostate



G.d.L. SBRT AIFM
S.Clemente

SBRT FOR PROSTATE the “current passion”

Volume 89 • Number 1 • 2014

Oncology Scan—Rising Stars, Fading Stars, and Shooting Stars: New Trends in Prostate Cancer Management

By Danny Y. Song, MD, Associate Editor

In this edition of Oncology Scan, Associate Editor Danny Song reviews 3 very provocative papers affecting the management of prostate cancer at different points along its evolution. The first report, by Thompson et al (1), looks at finasteride, the “fading star” of prostate cancer prevention; the second report investigates hypofractionation, the “current passion” of radiation oncologists for treatment of localized disease; and the third paper looks at radium-223 (²²³Ra), the “rising star” in skeletal metastatic disease. These practice-defining papers are testament to the numerous, high-quality, clinical research initiatives currently underway in this disease.

Fractionation schemes in SBRT Prostate

G.d.L.
SBRT

	TOTAL DOSE	DOSE Fx	N. Fx	OTT (Days)
EHF	33.5-50Gy	6.7-10Gy	4-5	4-29 days
MFH	51-72Gy	2.63-3.64Gy	14-30	19-45 days

EHF= Extreme Hypofractionation (<5 fx)
MHF= Moderate Hypofractionation (<35 fx)

Clinical outcome in SBRT Prostate



G.d.L.
SBRT

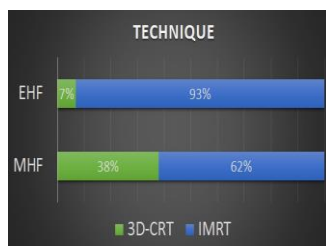
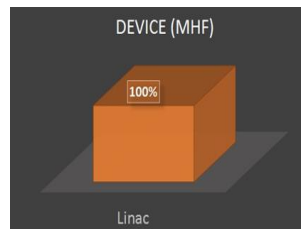
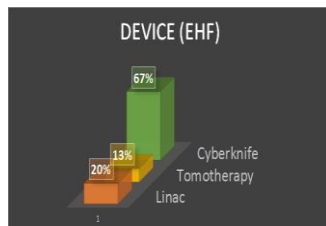
		EHF	MHF
4.8 y -bRFS	Low	86-100%	50-100%
	Intermediate	86-100%	56-100%
	High	78-100%	31-99%
Tox GU≥G2	Acute	1-45%	0-47%
	Late	1-20%	0-45%
Tox GI≥G2	Acute	0-21%	4-38%
	Late	0-28%	0-33%

G.d.L. SBRT AIFM
S.Clemente

Correlation of outcome
with technical aspect
such as imaging, immobilization,
margins...



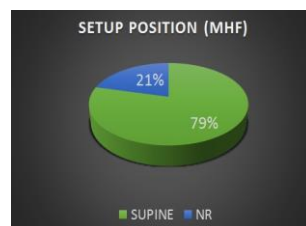
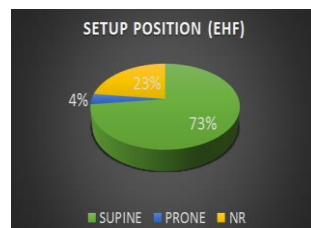
Device and technique in SBRT Prostate



G.d.L.
SBRT

G.d.L. SBRT AIFM
S.Clemente

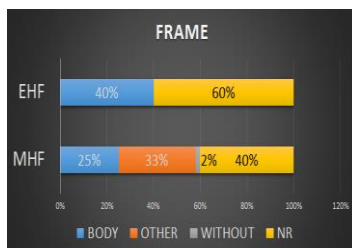
Set-up and frames in SBRT Prostate



G.d.L.
SBRT

G.d.L. SBRT AIFM
S.Clemente

Set-up and frames in SBRT Prostate



G.d.L.
SBRT

Rate of bRFS
higher
if frames were
used

10 Clemente et al.

International Journal of Radiation Oncology • Biology • Physics

Table 5 Biochemical relapse-free survival (bRFS) from studies at a median follow-up of 4.8 years

Parameter	Low risk			Intermediate risk			High risk		
	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)
FRAME Y	92.8	94.5	6.5	88.2	86	8.3	83.3	81.8	11.6
FRAME N	69.6	69.6	27.5	—	—	—	—	—	—

G.d.L. SBRT AIFM
S.Clemente

10 Clemente et al.

International Journal of Radiation Oncology • Biology • Physics

Table 5 Biochemical relapse-free survival (bRFS) from studies at a median follow-up of 4.8 years

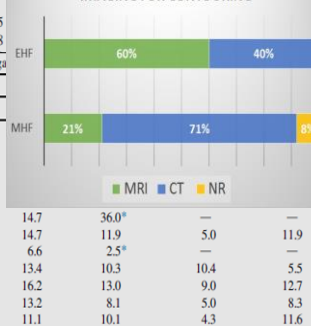
Parameter	Low risk			Intermediate risk			High risk		
	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)
FRAME Y	92.8	94.5	6.5	88.2	86	8.3	83.3	81.8	11.6
FRAME N	69.6	69.6	27.5	—	—	—	—	—	—
Rectum PREP Y	93.0	93.5	6.4	90.7	91	8.1	80.3	77.6	10.3
Rectum PREP N	—	—	—	79.0*	—	—	—	—	—
Bladder PREP Y	89.7	93.5	14.0	87.8	88.0	9.5	81.2	77.5	12.4
Bladder PREP N	94.4	94.0	5.3	93.9	94.8	7.2	90.4	92.0	10.5
MRI Y	94.2	96.4	7.2	93.6	95.0	8.5	88.7	89.0	10.5
MRI N	86.8	91.5	15.2	84.0	85.0	13.1	71.7	72.0	—
Only P Y	95.4	97.9	4.8	99.3	100.0	1.2	100	—	—
Only P N	86.1	91.3	16.0	83.7	84.0	12.7	75.6	77.5	—
MARG ≥ 5 mm Y	85.7	91.2	15.1	83.5	84.0	12.4	71.7	74.8	—
MARG ≥ 5 mm N	95.9	97.9	—	—	—	—	—	—	—
MARKERS Y	95.1	95.0	—	—	—	—	—	—	—
MARKERS N	87.0*	—	—	—	—	—	—	—	—
IMG3D Y	81.7	95.0	—	—	—	—	—	—	—
IMG3D N	93.4	94.0	—	—	—	—	—	—	—
IMGDAY Y	94.1	95.0	—	—	—	—	—	—	—
IMGDAY N	75.6	87.6	—	—	—	—	—	—	—
TRACK Y	95.8	97.7	—	—	—	—	—	—	—
TRACK N	87.9	91.7	—	—	—	—	—	—	—

Table 6 Acute and late grade ≥ 2 ($\geq G2$) genitourinary (GU) and GI toxicity

Parameter	$\geq G2$ GU toxicity	
	Mean (%)	Median (%)
Acute FRAME Y	21.4	19.0
Acute FRAME N	4.3*	—
Late FRAME Y	15.0	11.5
Late FRAME N	2.5	2.5
Acute PREP Y	19.7	13.9
Acute PREP N	18.9	16.3
Late PREP Y	13.9	7.0
Late PREP N	9.7	8.5
Acute MRI Y	21.4	22.0
Acute MRI N	19.8	13.8
Late MRI Y	15.9	11.5
Late MRI N	10.3	5.2

Great care has to be
taken to compensate
for prostate swelling if
segmentation was
performed with MRI-
only

IMAGING FOR CONTOURING



G.d.L.
SBRT



G.d.L. SBRT AIFM
S.Clemente

Table 5 Biochemical relapse-free survival (bRFS) from studies at a median follow-up of 4.8 years

Parameter	Low risk			Intermediate risk			High risk		
	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)
FRAME Y	92.8	94.5	6.5	88.2	86	8.3	83.3	81.8	11.6
FRAME N	69.6	69.6	27.5	—	—	—	—	—	—
Rectum PREP Y	93.0	93.5	6.4	90.7	91	8.1	80.3	—	—
Rectum PREP N	—	—	—	79.0*	—	—	—	—	—
Bladder PREP Y	89.7	93.5	14.0	87.8	88.0	9.5	81.2	—	—
Bladder PREP N	94.4	94.0	5.3	93.9	94.8	7.2	90.4	—	—
MRI Y	94.2	96.4	7.2	93.6	95.0	8.5	88.7	—	—
MRI N	86.8	91.5	15.2	84.0	85.0	13.1	71.7	—	—
Only P Y	95.4	97.9	4.8	99.3	100.0	1.2	100*	—	—
Only P N	86.1	91.3	16.0	83.7	84.0	12.7	75.6	—	—
MARG ≥ 5 mm Y	85.7	91.2	15.1	83.5	84.0	12.4	71.7	—	—
MARG ≥ 5 mm N	95.9	97.0	4.0	95.0	100.0	6.4	92.1	—	—
MARKERS Y	95.1	—	—	—	—	—	—	—	—
MARKERS N	87.0*	—	—	—	—	—	—	—	—
IMG3D Y	81.7	—	—	—	—	—	—	—	—
IMG3D N	93.4	—	—	—	—	—	—	—	—
IMGDAY Y	94.1	—	—	—	—	—	—	—	—
IMGDAY N	75.6	—	—	—	—	—	—	—	—
TRACK Y	95.8	—	—	—	—	—	—	—	—
TRACK N	87.9	—	—	—	—	—	—	—	—

G.d.L.
SBRT

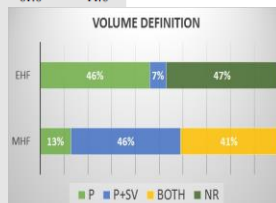


Table 6 Acute and late grade ≥ 2 ($\geq G2$) genitourinary (GU) and gastrointestinal (GI) toxicity

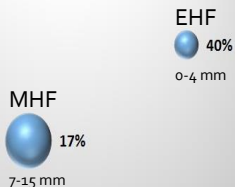
Parameter	$\geq G2$ GU toxicity			$\geq G2$ GI toxicity		
	Mean (%)	Median (%)	SD (%)	Mean (%)	Median (%)	SD (%)
Acute only P Y	15.8	13.0	13.8	7.6	6.0	6.0
Acute only P N	24.7	25.5	15.7	17.6	12.3	11.5
Late only P Y	12.1	11.0	11.7	10.2	6.0	11.0
Late only P N	14.3	12.0	13.4	10.2	5.0	10.6
Acute MARG ≥ 5 mm Y	22.3	22.0	16.5	15.7	12.2	12.2
Acute MARG ≥ 5 mm N	17.9	13.6	13.1	7.7	7.0	5.7
Late MARG ≥ 5 mm Y	13.6	9.5	13.3	11.2	5.0	10.8
Late MARG ≥ 5 mm N	11.1	9.0	9.3	6.4	2.3	8.5



G.d.L. SBRT AIFM
S.Clemente

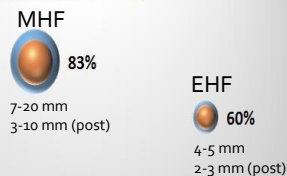
Margins in SBRT Prostate

ISOTROPIC MARGIN



Rate of Tox lower
and bRFS higher
if margins < 5mm

ANISOTROPIC MARGIN

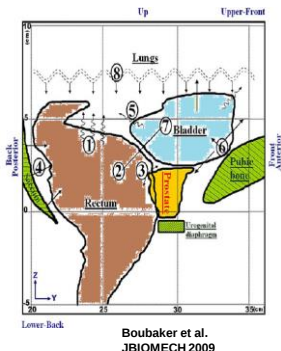


G.d.L.
SBRT



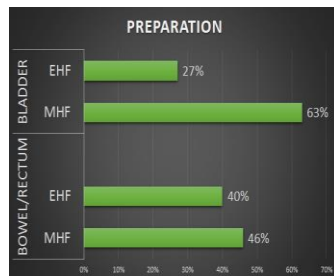
G.d.L. SBRT AIFM
S.Clemente

Organ motion: preparation in SBRT Prostate



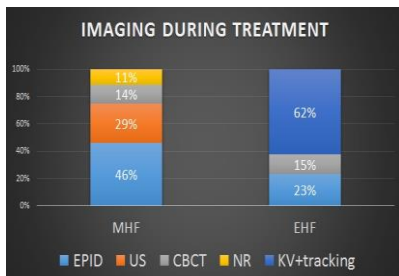
Rate of late $\geq G_2$ GU Tox
lower if preparation

G.d.L.
SBRT



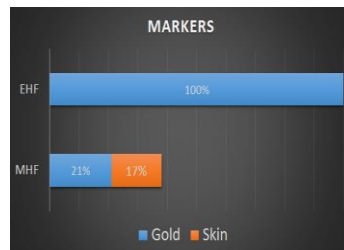
G.d.L. SBRT AIFM
S.Clemente

Imaging during treatment in SBRT Prostate



Daily imaging
and tracking have
a good impact
on Tox and bRFS

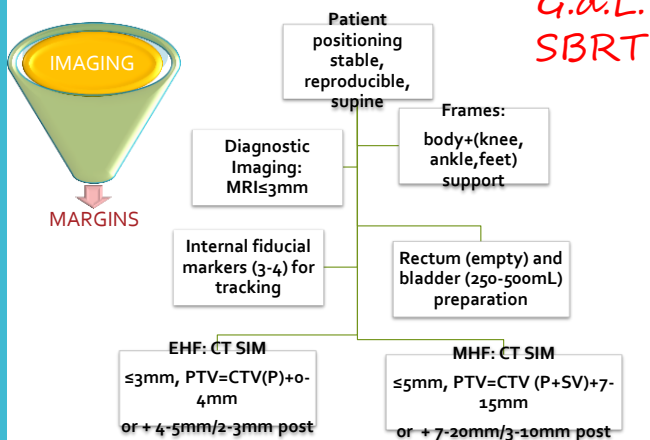
G.d.L.
SBRT



G.d.L. SBRT AIFM
S.Clemente

Imaging protocol for TVD in SBRT Prostate

PROSTATE



*G.d.L.
SBRT*

Ringraziamenti al Gruppo di Lavoro SBRT
"Imaging for target Volume Determination"

Valeria Landoni, IFO, Roma
Roberata Nigro, ASL Rieti
Caterina Oliviero, IRCCS CROB, Rionero in Vulture, PZ
Chiara Marchioni, ASL Rieti