STEREOTACTIC BODY RADIATION THERAPY

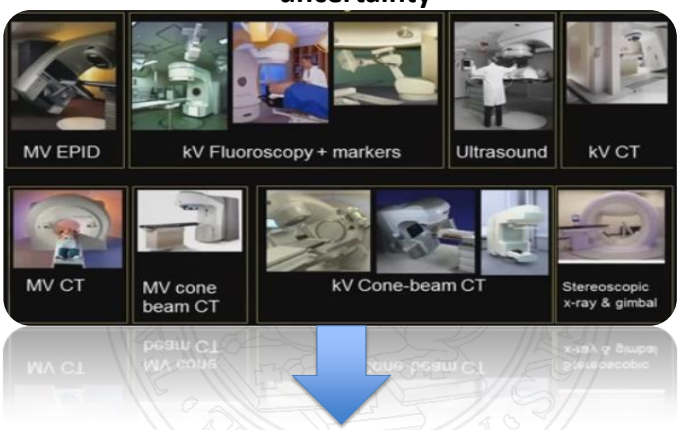
Implementazione, Sostenibilità, Avanzamento Tecnologico e Risultati a Confronto

24/25 Ottobre 2014, Mlano

Image Guided RT in SBRT

Christian Fiandra

IGRT provides the finest level of localization for inter-fraction uncertainty



reduce the spatial uncertainty

TARGET **OAR**

UNIVERSITA' DEGLI STUDI DI TORINO

Image Guided RT in SBRT

Considerations to the treatment-planning process

- **geometric performance** in terms of achievable accuracy
- **Application** to spine, lung, liver and prostate SBRT
- **replanning** based on information gained from image guidance

Without IGRT

	patient 1	patient 2	patient 3	patient 4	
fraction 1	0.5	0.0	0.2	0.7	
fraction 2	0.6	-0.5	0.3	0.2	
fraction 3	0.9	0.2	0.2	-0.4	
fraction 4	1.3	-1.1	0.3	-0.1	
mean	0.8	-0.4	0.3	0.1	mean =M
sd	0.3	0.6	0.1	0.5	SD = Σ
					RMS = σ

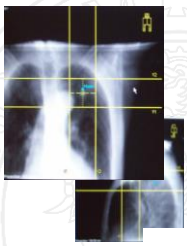
M = mean group error (equipment)
Σ = standard deviation of the inter-patient error
σ = standard deviation of the inter-fraction error
σf = standard deviation of the intra-fraction motion

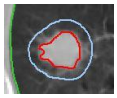
To cover the CTV for 90% of the patients with the 95% isodose (analytical solution) :

PTV margin = 2.5 Σ + 0.7 σ

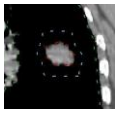
van Herk et al, IJROBP 47: 1121-1135, 2000

SBRT Without IGRT @ University of Torino





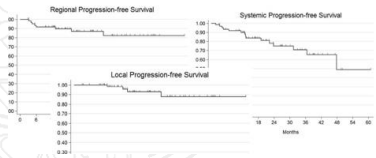
5 mm



10 mm

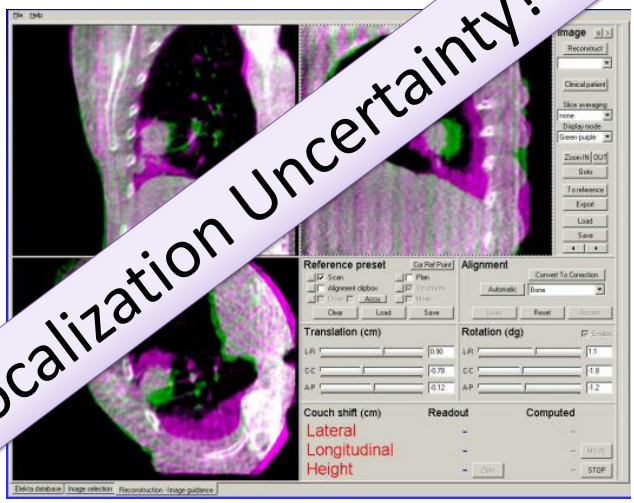
GTV=CTV
PTV

Progression-free Survival



Ricardi, Lung Cancer 2010

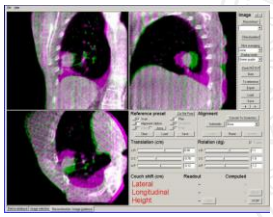
With IGRT…..

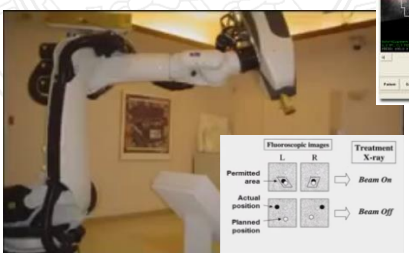


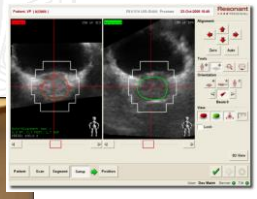
Localization Uncertainty?

IGRT uncertainties

- Target volume definition
- Inadequacy of surrogate used for IGRT
- Motion that cannot be corrected
- Too fast
- Too complex

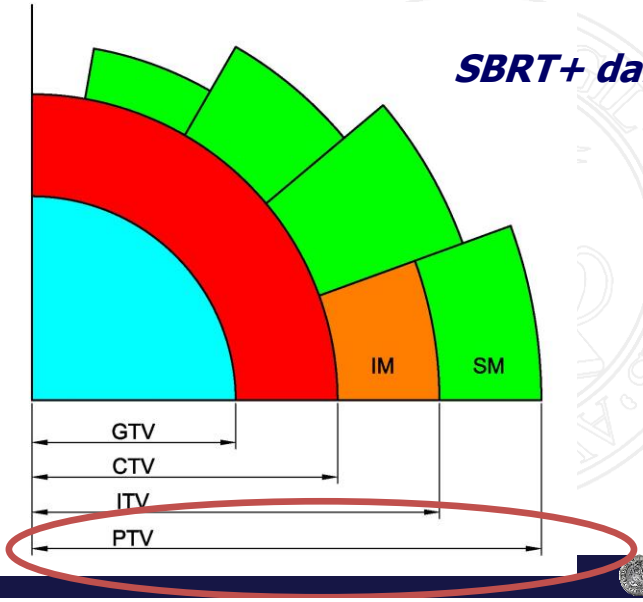






IGRT uncertainties

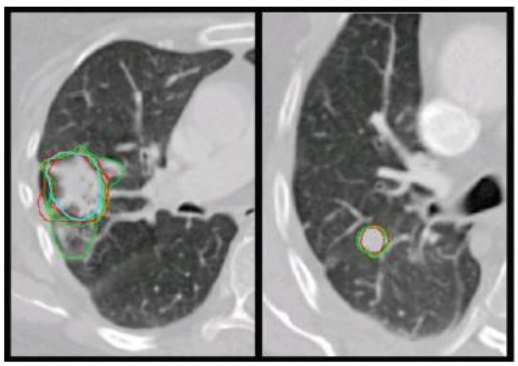
SBRT+ daily IGRT



1. Delineation uncertainties

The British Journal of Radiology, *85* (2012), e654–e660

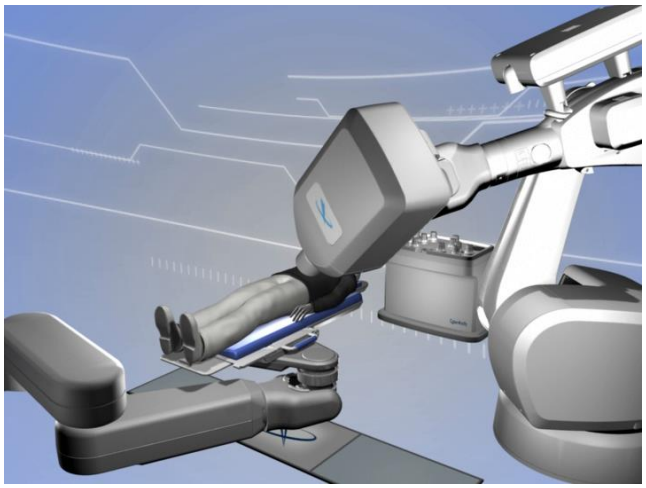
Interobserver delineation variation in lung tumour stereotactic body radiotherapy



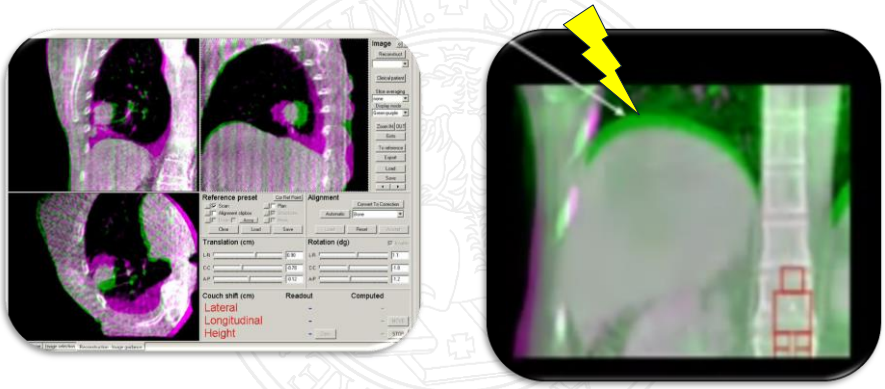
Conclusions

This is the first study to perform a systematic cross-sectional analysis of delineation variation for peripheral lung tumours treated with SBRT and quantified as SD to use for margin computation. We found a very small interobserver delineation variation in the transversal plane (2 mm, 1 SD) and larger in the cranio-caudal direction (3 mm, 1 SD) stressing that anisotropic margins should be applied.

2. Intrafraction uncertainty



3. Base-line shift uncertainty



Lung & Liver SBRT

Very clear lung tumor: IGRT hypo

all in cm	systematic errors	squared	random errors	squared
delineation	0.2	0.04		0
organ motion	0.1	0.01	0.1	0.01
setup error		0		0
Intra-fraction motion	0.15	0.0225	0.15	0.0225
respiration motion		0	0.7	0.444444
(0.33A)				
total error	0.27	0.07	0.69	0.476944
	times 2.5		difficult equation	
			non-linear	
error margin	0.67		0.22	
total error margin		0.89		

Using hypo-fractionation, prescription at 80% isodose line in lung

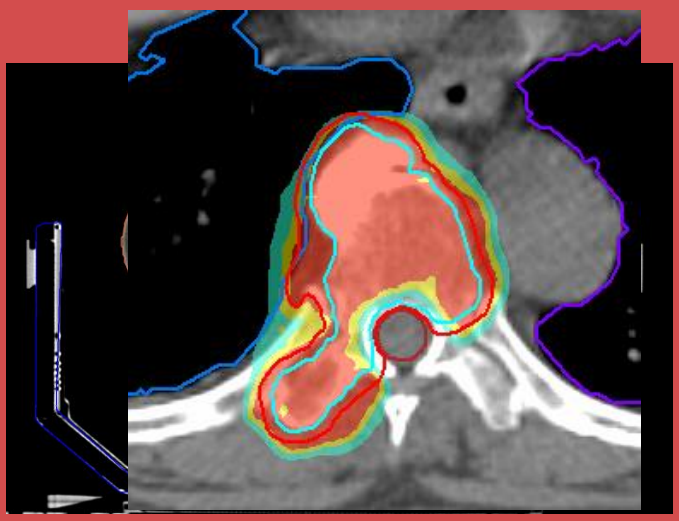
Courtesy of M. Van Herk

IGRT for…..

- SPINE SBRT
- LUNG SBRT
- LIVER SBRT
- PROSTATE SBRT

Spine SBRT

16 Gy / 1 fraction @ 95% isodose



Spine Stereotactic Body Radiotherapy Utilizing Cone-Beam CT Image-Guidance With a Robotic Couch: Intrafraction Motion Analysis Accounting for all Six Degrees of Freedom

Derek Hyde, Ph.D.,*,† Fiona Lochray, M.R.T.,* Renee Korol, Ph.D.,* Melanie Davidson, Ph.D.,* C. Shun Wong, M.D.,* Lijun Ma, Ph.D.,‡ and Arjun Sahgal, M.D.*,§

*Department of Radiation Oncology, Sunnybrook Health Sciences Centre, University of Toronto, Ontario, Canada; †British Columbia Cancer Agency, The Sindi Hawkins Cancer Centre for the Southern Interior, Kelowna, Canada; ‡Department of Radiation Oncology, University of California San Francisco, San Francisco, CA; and §Department of Radiation Oncology, Princess Margaret Hospital, University of Toronto, Toronto, Canada

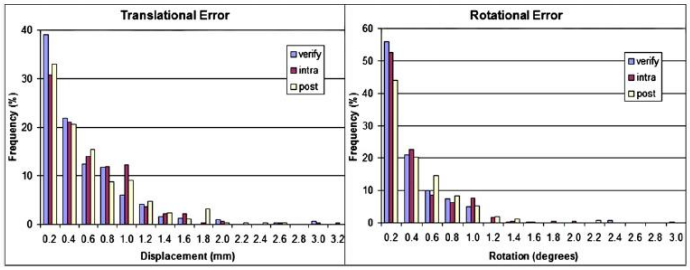
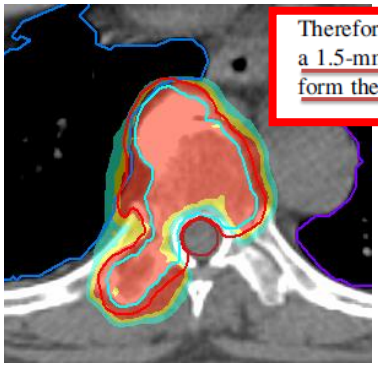


Fig. 2. Summary of translational and rotational residual errors, based on all 307 image registrations, according to the initial setup correction verification cone-beam CT (CBCT; verify), the intrafractional CBCT (intra), and the posttreatment CBCT (post). There were no statistically significant differences between each direction, so the absolute errors for each direction have been binned together for simplicity.

Spine SBRT

For the entire cohort (307 image registrations), the translational and rotational errors in patient positioning were found to be relatively small, where 90% were within 1 mm and 97% within 1°. However, there were occasional larger positioning errors observed with 1.6% and 0.8% of the registrations indicating ≥2 mm and ≥2° deviations in position, respectively. These data are in good agreement with those reported in the literature for patients treated with spine SBRT and immobilized in the BodyFIX system (12, 15,



Therefore, we are confident in our current practice of applying a 1.5-mm margin to the clinical target volume and spinal cord to form the PTV and cord PRV, respectively (2, 16).

Conclusion

We report the ability to maintain the position of a spine SBRT target to within 1.2 mm and 0.9° (95% confidence) when patients are immobilized in a near-rigid body immobilization device, setup is based on CBCT image guidance, intrafraction CBCT images are acquired at approximately 20-min time intervals, a threshold of 1 mm and 1° is used for repositioning, and corrections are performed in all 6-DOF.

Spine SBRT

RTOG 0631 Protocol Information

Phase II/III Study of Image-Guided Radiosurgery/SBRT for Localized Spine Metastasis---RTOG CCOP Study

Protocol Documents

Protocol **Current Version Date:** 4/21/2014

Informed Consent

Summary of Changes

Track Amendments/ Update

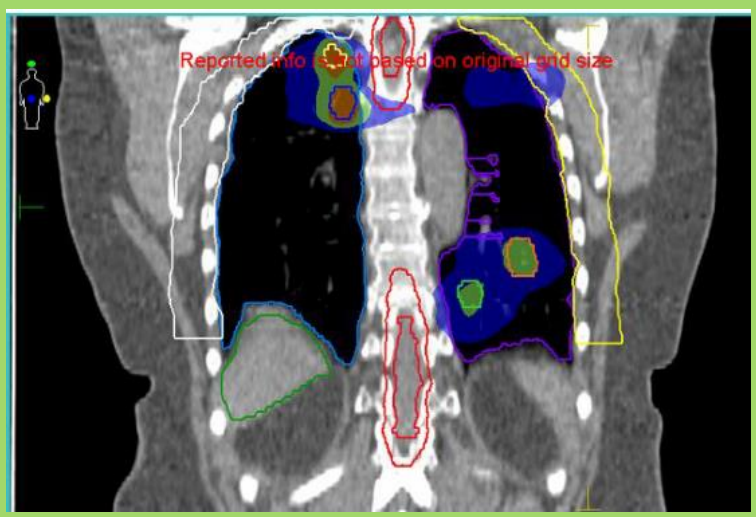
Case Credits/Reimbursement Info

Principal Investigator: Samuel Ryu, MD

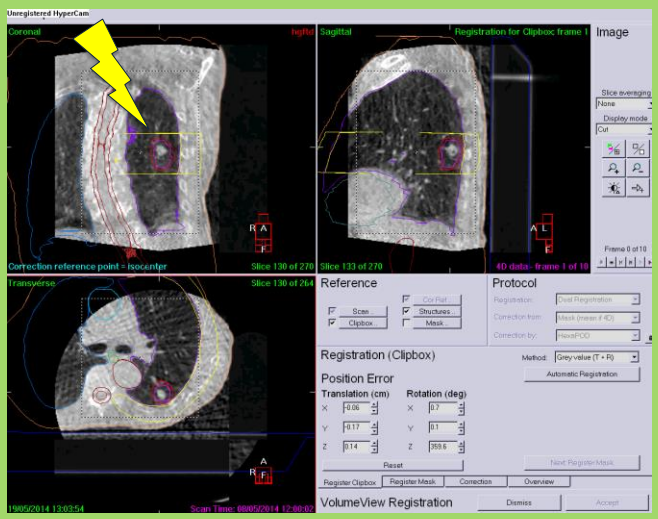
Primary Objective:
Phase II Component: Determine the feasibility of successfully delivering image-guided radiosurgery/SBRT for metastases in a cooperative group setting.
Phase III Component: Determine whether image-guided radiosurgery/SBRT (single dose of 16 Gy) improves measured by the 11 point NRPS) as compared to conventional external beam radiotherapy (single dose of 8 Gy).

2 mm margin from CTV to PTV

Lung SBRT



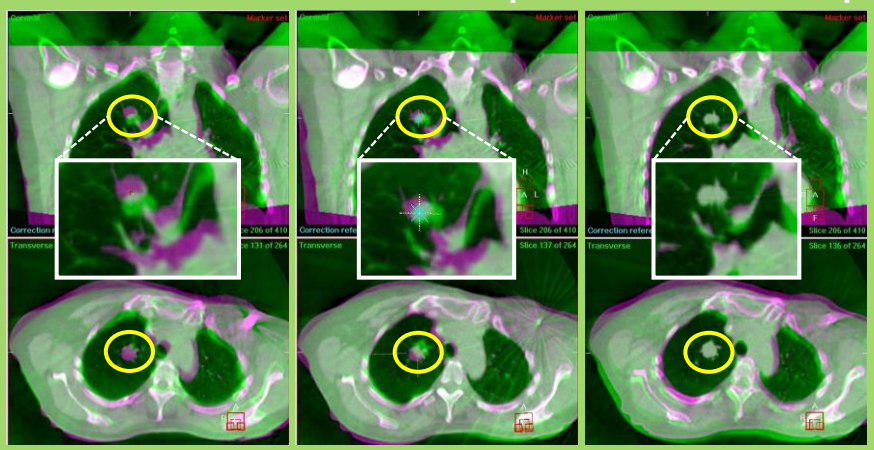
Lung SBRT



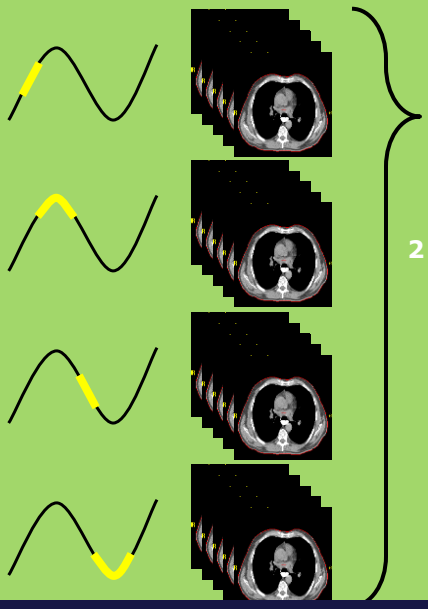
Sonke J-J Med Phys 2005;

Lung SBRT

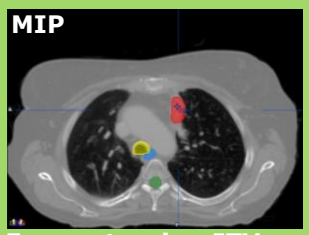
Skin marks | Bone set-up | Soft-tissue set-up



Lung SBRT – CT scanner



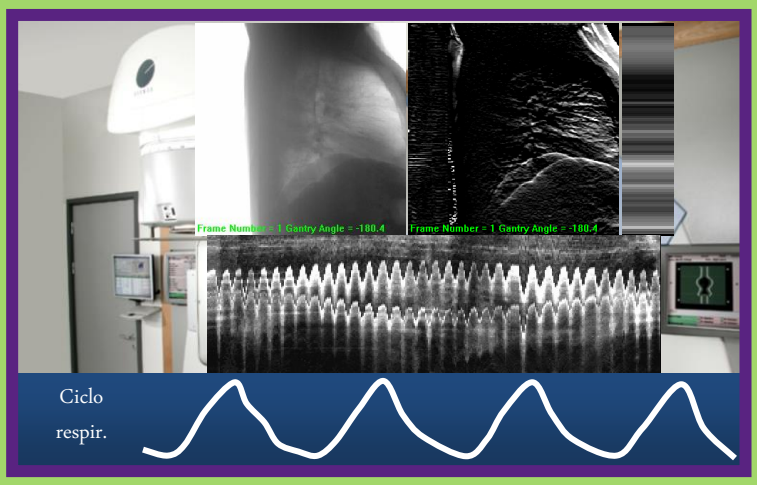
2 Datasets



For contouring ITV

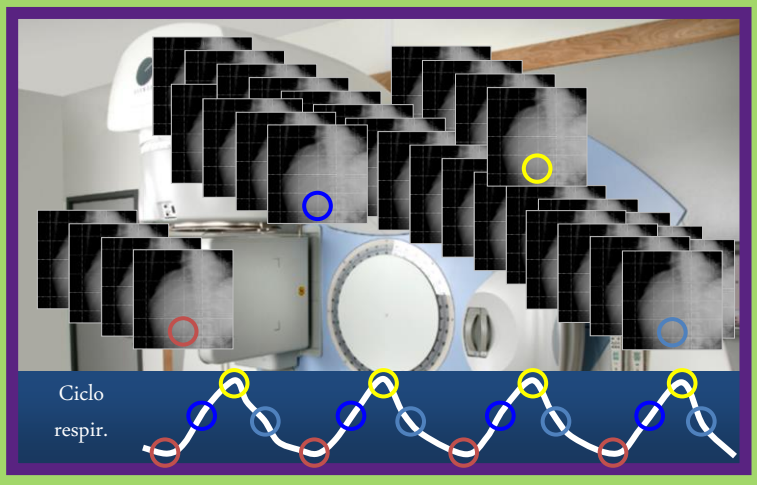
For dose calculation and reference IGRT image

Lung SBRT – 4D CBCT

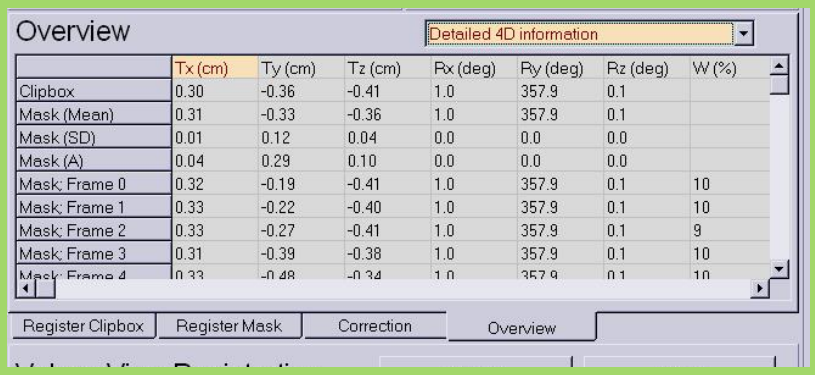


Lung SBRT – 4D CBCT

Lung SBRT – 4D CBCT



Lung SBRT – 4D CBCT



	Tx (cm)	Ty (cm)	Tz (cm)	Rx (deg)	Ry (deg)	Rz (deg)	W (%)
Clipbox	0.30	-0.36	-0.41	1.0	357.9	0.1	
Mask (Mean)	0.31	-0.33	-0.36	1.0	357.9	0.1	
Mask (SD)	0.01	0.12	0.04	0.0	0.0	0.0	
Mask (A)	0.04	0.29	0.10	0.0	0.0	0.0	
Mask; Frame 0	0.32	-0.19	-0.41	1.0	357.9	0.1	10
Mask; Frame 1	0.33	-0.22	-0.40	1.0	357.9	0.1	10
Mask; Frame 2	0.33	-0.27	-0.41	1.0	357.9	0.1	9
Mask; Frame 3	0.31	-0.39	-0.38	1.0	357.9	0.1	10
Mask; Frame 4	0.33	-0.48	-0.34	1.0	357.9	0.1	10

Lung SBRT – IGRT achievable accuracy

PHYSICS CONTRIBUTION

FRAMELESS STEREOTACTIC BODY RADIOTHERAPY FOR LUNG CANCER USING FOUR-DIMENSIONAL CONE BEAM CT GUIDANCE

JAN-JAKOB SONKE, PH.D.,* MADDALENA ROSSI, R.T.T.,* JOCHEM WOLTHAUS, M.SC.,* MARCEL VAN HERK, PH.D.,* EUGENE DAMEN, PH.D.,* AND JOSE BELDERBOS, M.D., PH.D.*

*Department of Radiation Oncology, The Netherlands Cancer Institute-Antoni van Leeuwenhoek Hospital, Amsterdam, The Netherlands

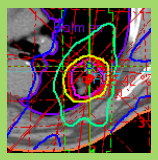
4D-CBCT guidance. The group mean, systematic, and random localization errors (*i.e.*, discrepancies between planned and actual tumor position after corrections applied) were <1.5 mm for each directions, whereas the group mean systematic, and random intrafraction variability were <2 mm, despite the absence of aggressive immobilization. In con-

Table 4. Amplitudes and PTV margins of the 10 patients used in the Monte Carlo error simulation

	Amplitude (mm)			Margin (mm)		
Patient No.	Left-right	Craniocaudal	Anteroposterior	Left-right	Craniocaudal	Anteroposterior
1	1.6	2.1	1.7	5.8	5.8	6.4
2	2.4	2.6	1.2	5.8	5.9	6.3
3	1.0	4.0	2.9	5.8	5.9	6.4

Lung SBRT – IGRT achievable accuracy

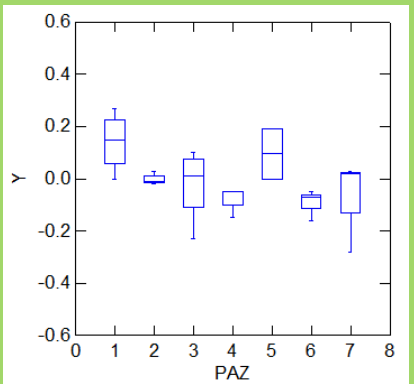
@ University of Torino



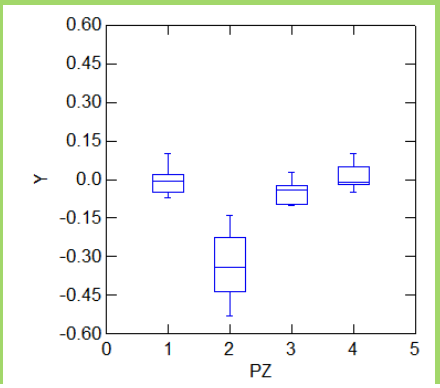
PTV = ITV + 3 mm isotropic

3 mm

Inter-fraction

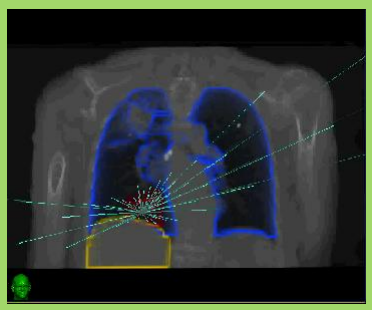


Intra-fraction



Lung SBRT – cyberknife

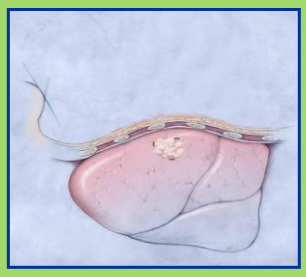
- Tightly contoured beams following tumor motion in real-time
- Delivers radiation throughout the respiratory cycle without gating or breath-holding
- Continuously adapts to variations in breathing patterns
- Maximizes healthy tissue sparing relative to IMRT / IGRT
- Proven accuracy
  - Respiratory motion targeting accuracy of 0.70 +/- 0.33mm* **



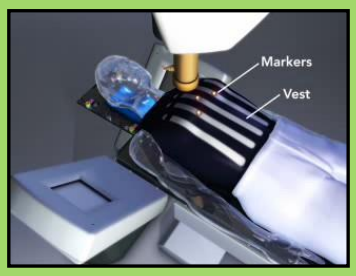
* Reference: Dieterich S, Taylor D, Chuang C, Wong K, Tang J, Kilby W, Main W. The CyberKnife® Synchrony Respiratory Tracking System: Evaluation of Systematic Targeting Uncertainty.
**Synchrony System clinical accuracy specification of 1.5 mm for moving targets.

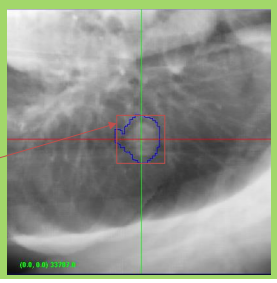
Lung SBRT – cyberknife

Fiducials, implanted prior to treatment



Optical markers on a special patient vest

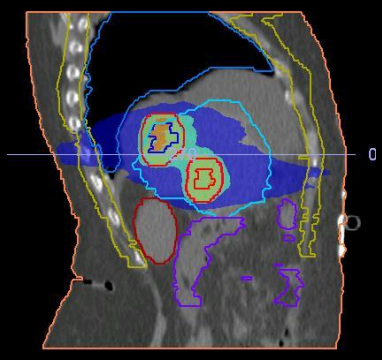




Matching window

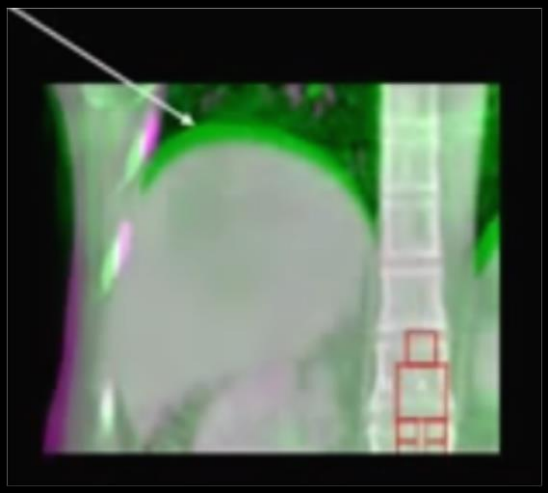
Direct soft tissue tracking

Liver SBRT



- ❑ **Tumor dose often limited by normal tissue tolerances:**
  - ➢ **Volume liver irradiated**
  - ➢ **Proximity to luminal GI organs**
- ❑ **Strong motivation for reduced PTV**
- ❑ **Need for advanced technologies + IGRT**

Liver SBRT
Baseline shift in Liver position

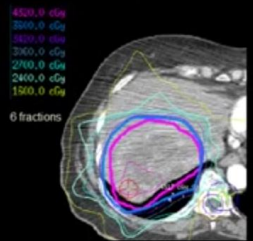


Shift in Liver position relatve to vertebral bodies

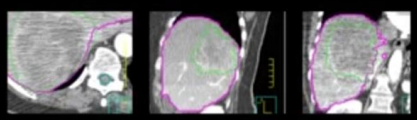
Liver SBRT
Baseline shift in Liver position

- Change of Position of Spinal Cord Relative to Liver Detected

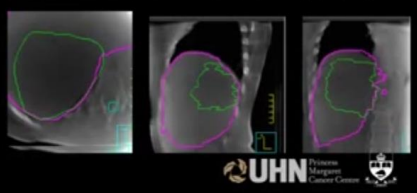
- Liver-liver match led to higher spinal cord dose, requiring replan



Planning CT, with liver, cord and GTV contours



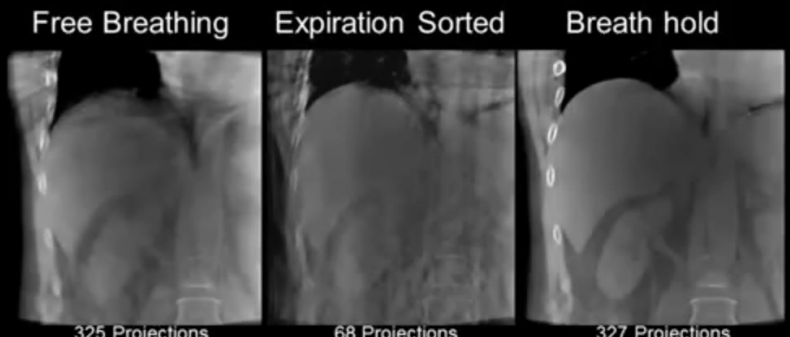
Cone beam CT, with contours from planning CT



Courtesy of Dr. L.Dawson

Liver SBRT

kV CBCT – Breathing Motion

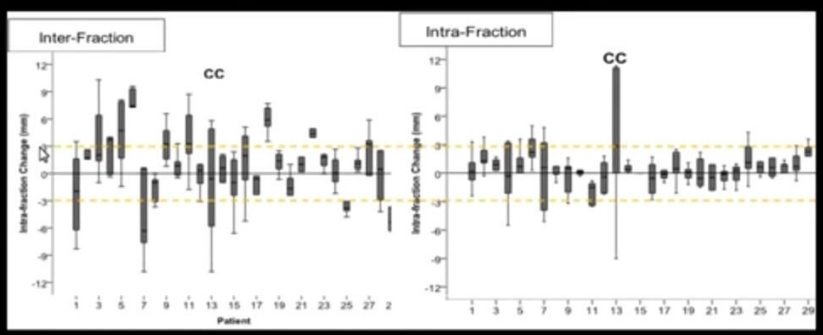


Courtesy of Dr. L.Dawson

Liver SBRT

Non-Breath Hold Liver Shifts

Sup/inf Liver Relative to Vertebral Bodies



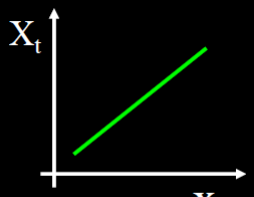
- Inter-fraction shifts > intra-fraction shifts
- 314 respiratory sorted CBCT from 29 pts, 6 fraction SBRT, non-breath hold
- Intra-fraction time [min:sec]: Mean 12.16 (4:56 – 25:37)

Courtesy of Dr. L.Dawson

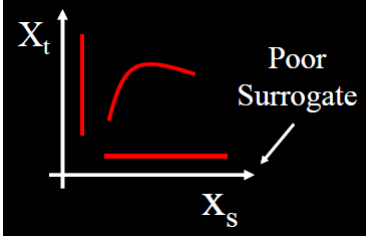
LIVER SBRT
Surrogates for repositioning

For all imaging techniques, the tumor is often difficult, if not impossible, to visualize, leading image guidance techniques to rely on surrogates for positioning the liver tumor

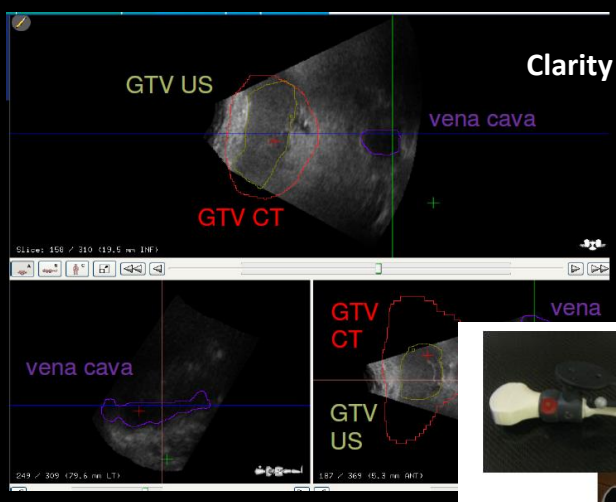
- ***fiducial markers***
- ***Calcifications***
- ***Surgical clips***
- ***Large vessels***
- ***Entire liver or individual lobes***



High Quality Surrogate



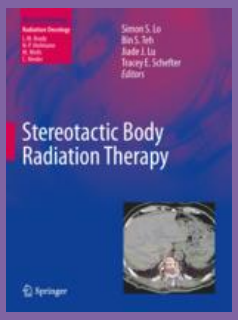
3D US imaging for liver lesions



Clarity 3DUS system (Elekta)

Courtesy of Maastro Clinic

Prostate SBRT



tate SBRT. Generally, a PTV margin of 3–5 mm is used for prostate SBRT. It is noteworthy that most institutions use real-time motion tracking system provided by the CyberKnife system ("CyberKnife System"). Larger margin may be needed if no real-time motion tracking is available.

Table 4 Reported margin size, PTV constraints, and type of machine

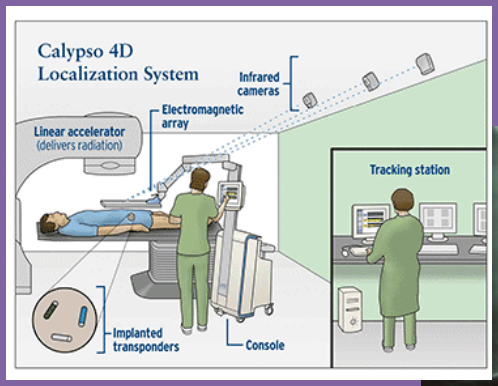
Author	Institution	Machine	Margin size	PTV constraints
Madsen et al. (2007)	Virginia Mason Medical Center	Conventional linear accelerator	4–5 mm from prostate to block edge	100 % isocenter prostate covered by 90 % isodose line
Freeman and King (2011)	Stanford University and Naples Radiation Oncology	CyberKnife	GTV = prostate and proximal 1 cm of seminal vesicle CTV = GTV + 3 mm anteriorly and laterally, 1 mm posteriorly. PTV = CTV + 2 mm anteriorly, laterally, and posteriorly	95 % of PTV covered by prescription dose
Tang et al. (2008)	University of Toronto	Conventional linear accelerator	CTV = Prostate PTV = CTV + 4 mm	100 % of CTV $\geq$ 35 Gy 99 % of PTV $\geq$ 33.25 Gy Max $\leq$ 105 %
Friedland et al. (2009)	Naples Radiation Oncology	CyberKnife	GTV = Prostate and proximal 1 cm of seminal vesicle PTV = GTV + 3 mm posteriorly and 5 mm all other directions	95 % of PTV covered by prescription dose
Katz et al. (2010)	Winthrop-University Hospital	CyberKnife	GTV for low risk = Prostate GTV for intermediate, high risk = Prostate + half of seminal vesicle PTV for low, intermediate risk = GTV + 3 mm posteriorly and 5 mm all other directions PTV for high risk = GTV + 3 mm posteriorly, 8 mm involved side, 5 mm all other directions	96 % of PTV covered by prescription dose
Bolzicco et al. (2010)	San Bortolo Hospital, Italy	CyberKnife	GTV = Prostate PTV = GTV + 3 mm posteriorly and 5 mm all other directions	95 % of PTV covered by prescription dose
Jabbari et al. (2012)	UCSF	CyberKnife	CTV = Prostate +seminal vesicle PTV = CTV ± 2 mm (no overlap with rectum)	HDR-like planning Prescription isodose is in 60–80 % range
Boike et al. (2011)	UT Southwestern Medical Center	Tomotherapy or Conventional linear accelerator	CTV = Prostate PTV = CTV + 3 mm	95 % of PTV covered by prescription dose
Oermann et al. (2011)	Georgetown University	CyberKnife	GTV = Prostate CTV = Prostate +proximal seminal vesicle PTV = CTV + 3 mm posteriorly and 5 mm all other directions	95 % of PTV covered by prescription dose
King et al. (2011)	UCLA/Stanford University	CyberKnife	PTV = Prostate + 3 mm posteriorly and 5 mm all other directions	95 % of PTV covered by prescription dose

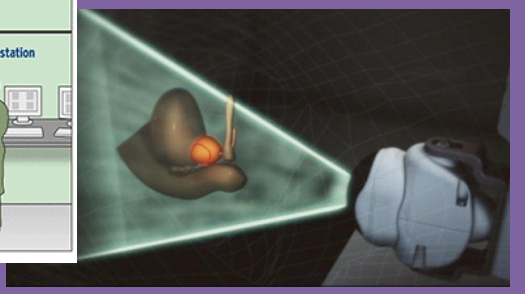
Prostate SBRT

Real time tracking 1

Prostate SBRT

Real time tracking 2





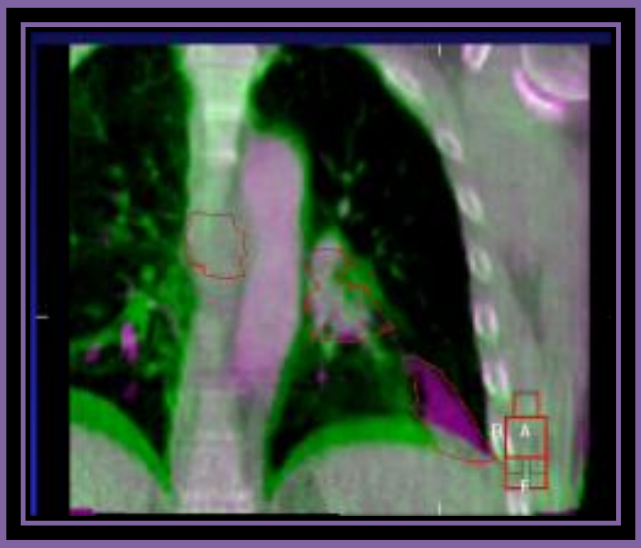
Prostate SBRT

Prostate: 2.5 Σ + 0.7 σ
Now add IGRT

all in cm	systematic errors	squared	random errors	squared	
delineation	0.25	0.0625	0	0	Rasch et al, Sem. RO 2005
organ motion	0	0	0	0	van Herk et al, IJROBP 1995
setup error	0	0	0	0	Bel et al,IJROBP 1995
intrafraction motion			0.1	0.01	
total error	0.25	0.06	0.10	0.01	
	times 2.5		times 0.7		
error margin	0.63		0.07		
total error margin		0.70			

Engels et al (Brussels, 2010) found 50% recurrences using 3 mm margin with marker IGRT

Courtesy of M. Van Herk



IGRT not able to solve this problem…

Courtesy of J-J Sonke

Volumetric IGRT images may be used also for determination of accumulated delivered dose versus planned dose:

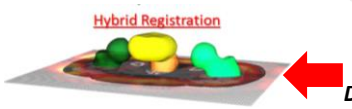
IGART

It is a common practice in adaptive radiotherapy to collect Cone-Beam Computed Tomography (CBCT) on a daily basis throughout the course of treatment

Image Guided Adaptive RT
IGART

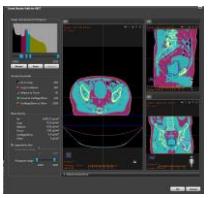
necessary to register daily images with planning images and to deform contours and doses in order to monitor the actual dose delivered to the organs

Dose Accumulation

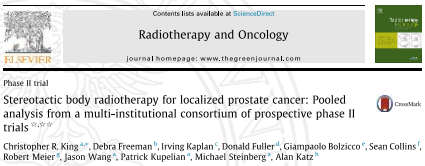


Dose Deformation

Dose Recalculation



- **Stereotactic radiotherapy for prostate cancer**
  - **5 patients**
- **Treatment PLAN:**
  - IGRT/IMRT
  - 37,5 Gy (7,5 Gy per fraction)
- **DAILY IMAGING:** 5 CBCTs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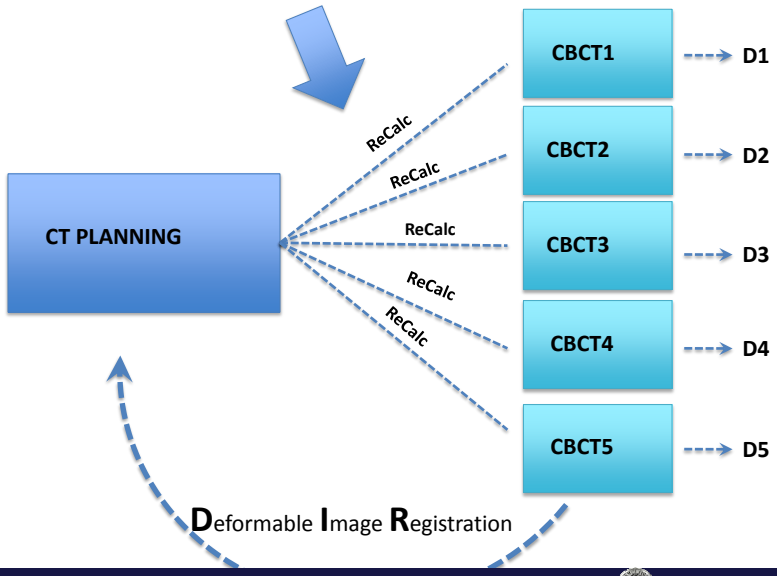
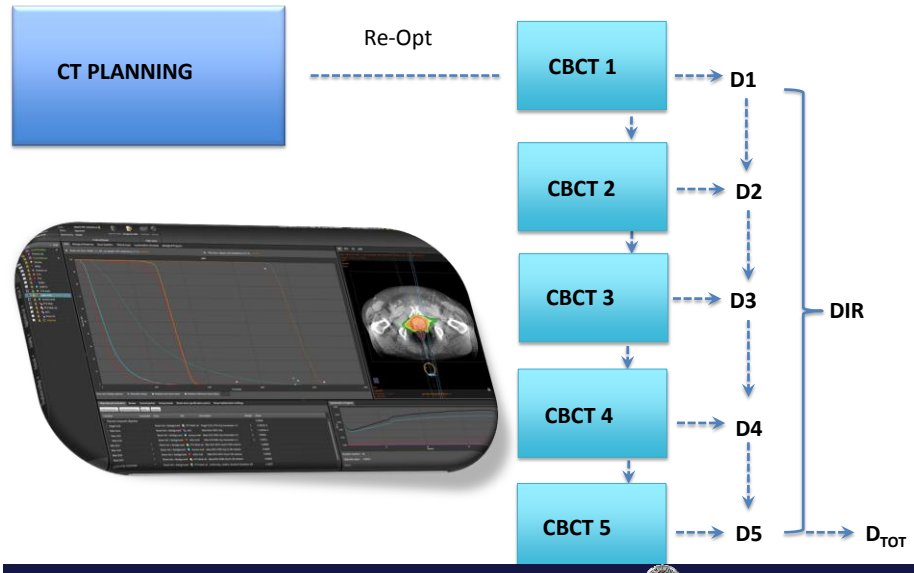
ELSEVIER
Phase II trial
Stereotactic body radiotherapy for localized prostate cancer: Pooled analysis from a multi-institutional consortium of prospective phase II trials ☆,☆☆
Christopher R. King [a,*], Debra Freeman [b], Irving Kaplan [c], Donald Fuller [d], Giampaolo Bolzicco [e], Sean Collins [f], Robert Meier [g], Jason Wang [h], Patrick Kupelian [a], Michael Steinberg [a], Alan Katz [a]

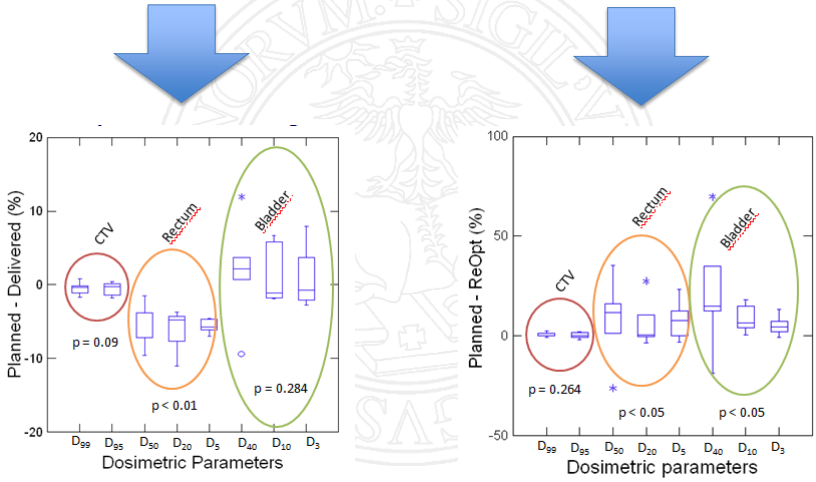
Dose tracking Vs Re-Optimization



Dose tracking Vs Re-Optimization



Dose tracking Vs Re-Optimization



Conclusions

Daily on-line IGRT corrections recommended for SBRT treatments

In spite of different system of IGRT there are still uncertainties that need to be covered by safety margins

If the patient's anatomy changes, IGRT images should be evaluated also for Adaptive Planning

IGRT and ART increase the precision of radiotherapy and thus have the potential to increase the therapeutic window

Ringraziamenti

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Dr. G. Beltramo – CDI – Milano
U. Ricardi, A.R. Filippi, S. Badellino, A. Guarneri, E. Trino, F. Munoz, S. Bartoncini - Torino

TECNOLOGIE AVANZATE