Congresso Inter-regionale
AIRO Lombardia e AIRO Piemonte-Liguria-Valle d'Aosta

L'INNOVAZIONE TECNOLOGICA IN RADIOTERAPIA: NUOVI STANDARD CLINICI E PROBLEMATICHE GESTIONALI

Centro Congressi VILLA CAGNOLA
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Sabato 29 novembre 2014

IGRT: in quali patologie e con quali tecnologie?

Marco Krengli

Università del Piemonte Orientale
AOU Maggiore della Carità
Novara

UPO UNIVERSITÀ DEL PIEMONTE ORIENTALE

IMPORTANCE OF IGRT

IGRT: tools for verifying patient position and adapting treatment plans.
It is central to the management of cancer patients being treated by RT.

DOSE prescription

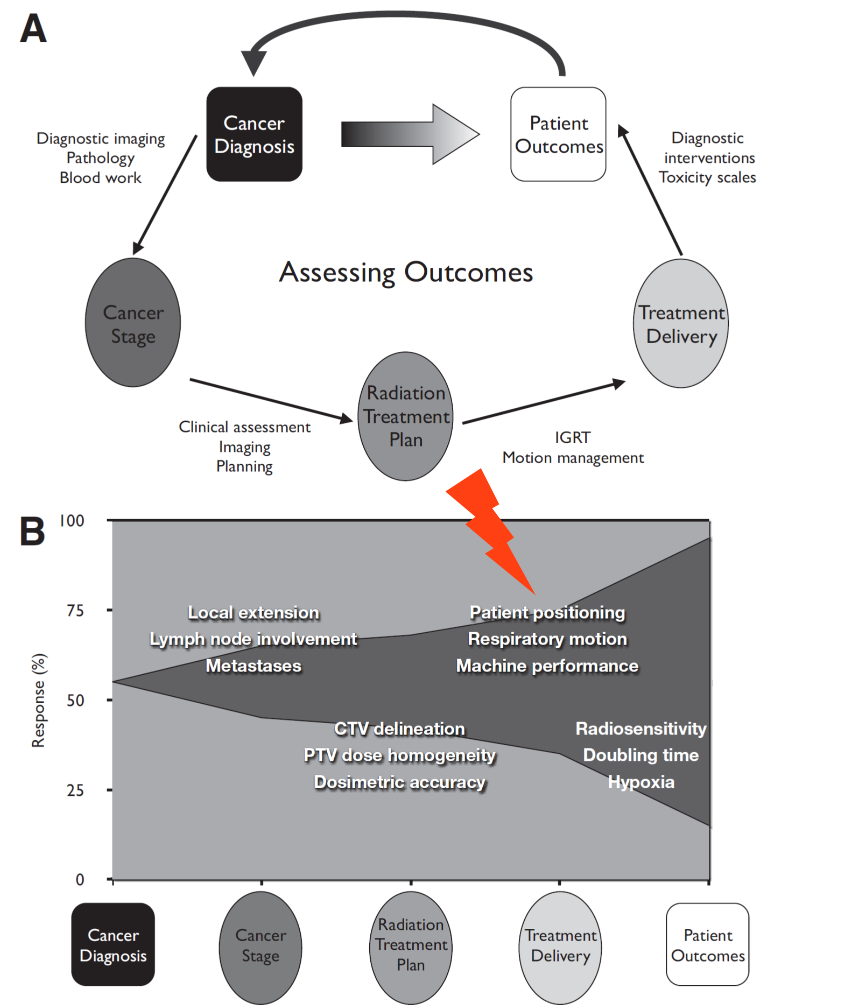
Target delineation

TCP

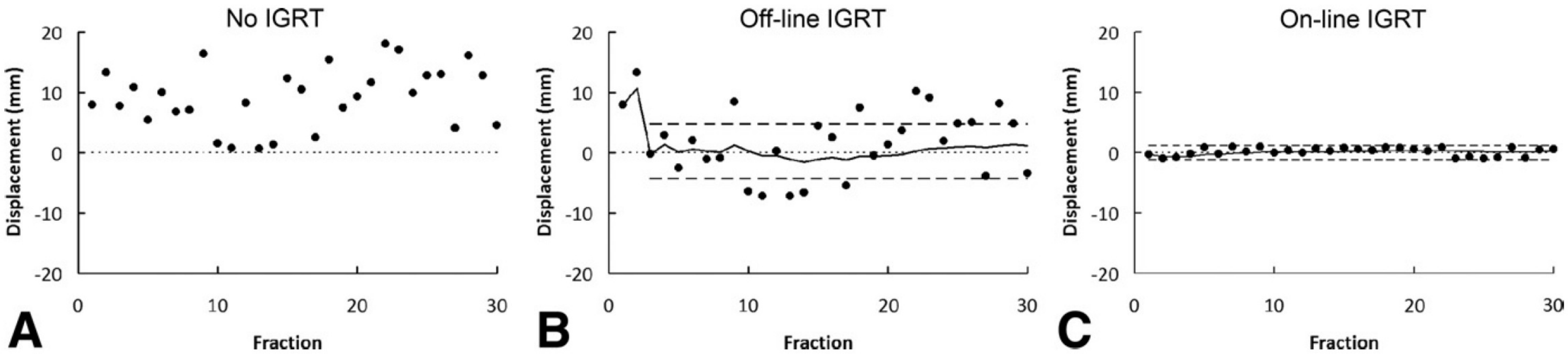
IGRT

Delivery accuracy 3D-IMRT-STR

NTCP



IMPORTANCE OF IGRT



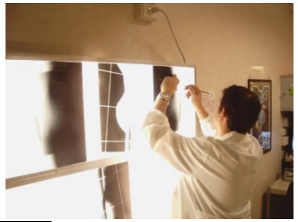
THE TREATMENT OF THE "DAY"

Bujold A, Semin Radiat Oncol 2012

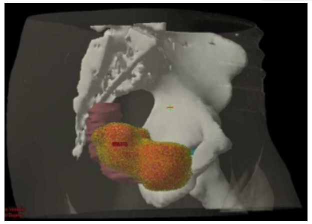
IGRT is not a new concept

1D: navigation with eyes

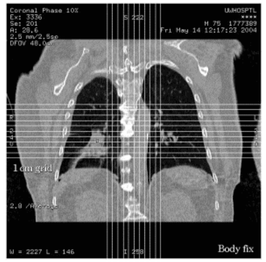
2D: navigation in a plane



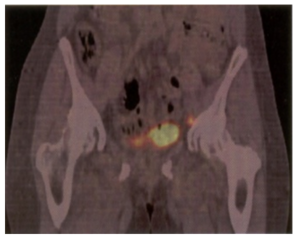
3D: navigation in a Volume



4D: navigation in the Time



5D: navigation in the Biology



3-D imaging acquisition

CT
kV-MV

Examples:
CBCT, CT on-rail, Tomo

Average dose/fr:
10-50 mGy

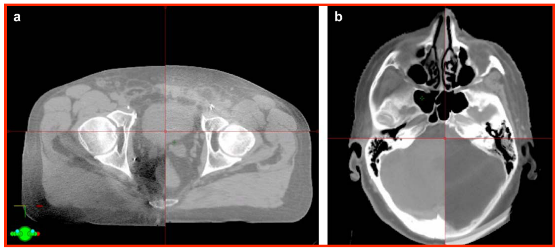
Accuracy:
<1 mm

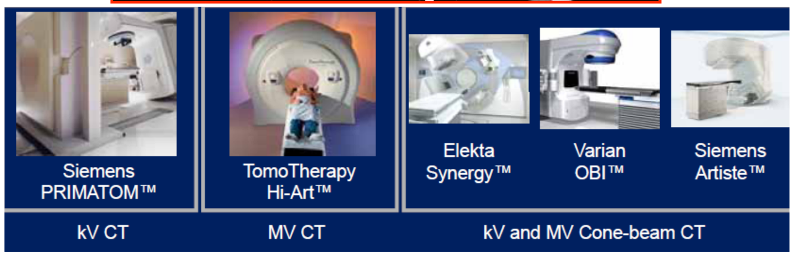
Routine clinical use:
localization based on volumetric image acquisition and 3D-3D matching with treatment planning CT

Sites commonly applied:
SBRT/SRS
thorax, liver, brain, H&N, spine

Benefits: monitoring patient setup (interfraction motion), changes in anatomy during treatment, and monitor tumor response through course of therapy; useful fiducials

Caveat: dose, artifacts





De Los Santos J et al, Critical Review, IJROBP 2013,

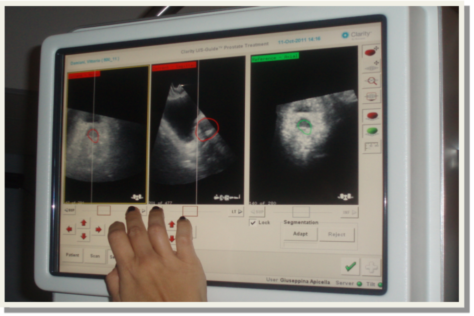
3-D imaging acquisition

ultrasound

Examples:
BAT, SonArray, iBEAM, RESTITU/Clarity
Average dose/fr:
no extra dose
Accuracy:
3-5 mm
Routine clinical use:
alignment of target to decrease interfraction setup errors
Sites commonly applied:
prostate, breast

Benefits: non-ionizing; real-time assessment of intrafraction motion will soon be possible with 4-D ultrasound

Caveat: potential higher inter-users variability



De Los Santos J, Critical Review, IJROBP 2013

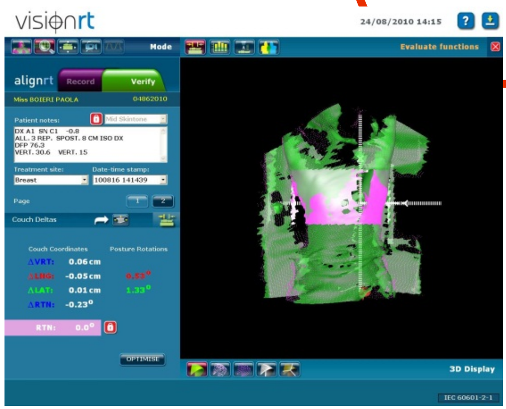
3-D imaging acquisition

Camera-based

Examples:
Align-RT
Average dose/fr:
no extra dose
Accuracy:
1-2 mm
Routine clinical use:
used for surface-based localization
Sites commonly applied:
breast, abdomen, pelvis, H&N

Benefits: non-ionizing, gating is also possible based on respiratory monitoring of an external surrogate. Fast

Caveat: Only setup verification; more useful if the surface serves as a good surrogate for localization of the target



De Los Santos J, Critical Review, IJROBP 2013

4-D imaging acquisition

X-ray real time tracking systems
Combined infrared
+
ortogonal kV

Examples:
ExacTrac, CyberKnife
Average dose/fr:
0.1-200mGy
Accuracy:
Routine clinical use:
Tumor tracking, tumor position - external markers, updated during treatment using kV orthogonal imaging
Sites commonly applied:
any SBRT/SRS

Benefits: Correlation between external markers and internal tumor motion helps circumvent possible phase offsets;

Caveat: dose; implantation of markers, if required, is an invasive procedure

De Los Santos J, Critical Review, IJROBP 2013

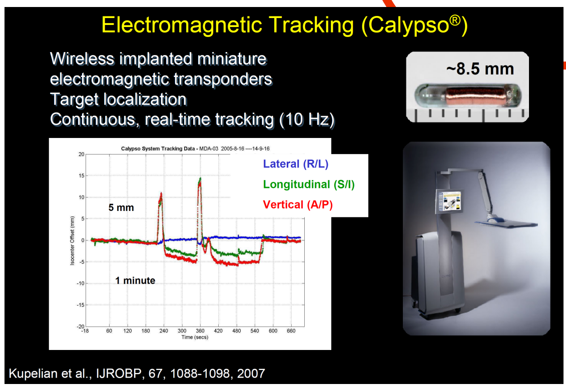
4-D imaging acquisition

nonX-ray 4D
Traking systems

Examples:
Calypso
Average dose/fr:
no extra dose
ectromagnetic
Accuracy:
indipendent from linac
Routine clinical use:
Electromagnetic transponders implanted in the prostate gland, intrafraction motion
Sites commonly applied:
prostate

Benefits: Real-time assessment of intrafraction motion of the prostate gland;
radiation beam can be halted if transponder motion is outside a predefined tolerance, thereby improving localization accuracy in
"real time"

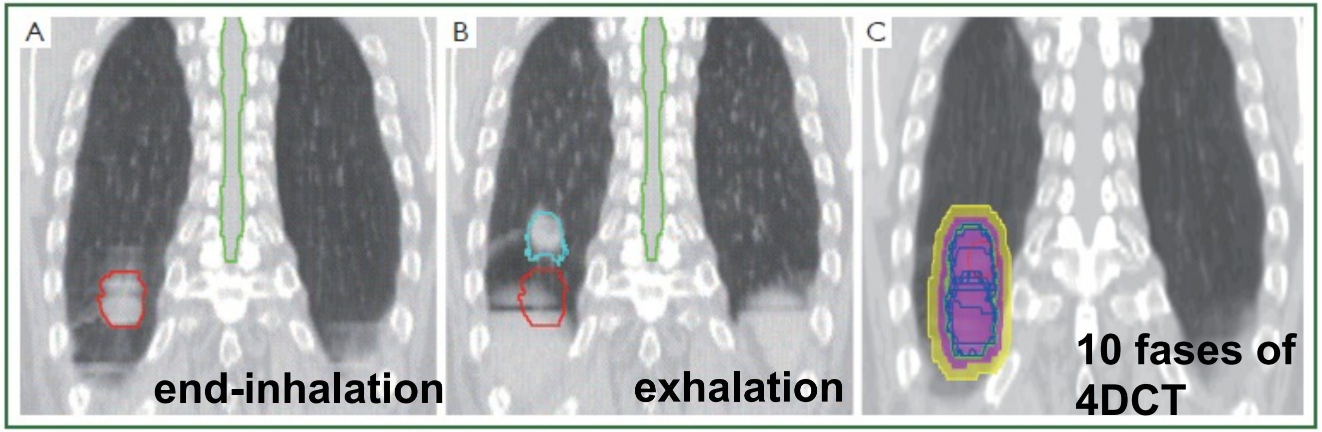
Caveat: implantation of transponders in the prostate is considered invasive;
transponders cause artifacts on MR images



De Los Santos J, Critical Review, IJROBP 2013

THE LUNG ISSUE

THE AIM: To reduce the ITV especially in the setting of SBRT



For locally advanced stage NSCLC, typical margins for the PTV are in the order of 5-10 mm if an ITV is used for motion compensation.

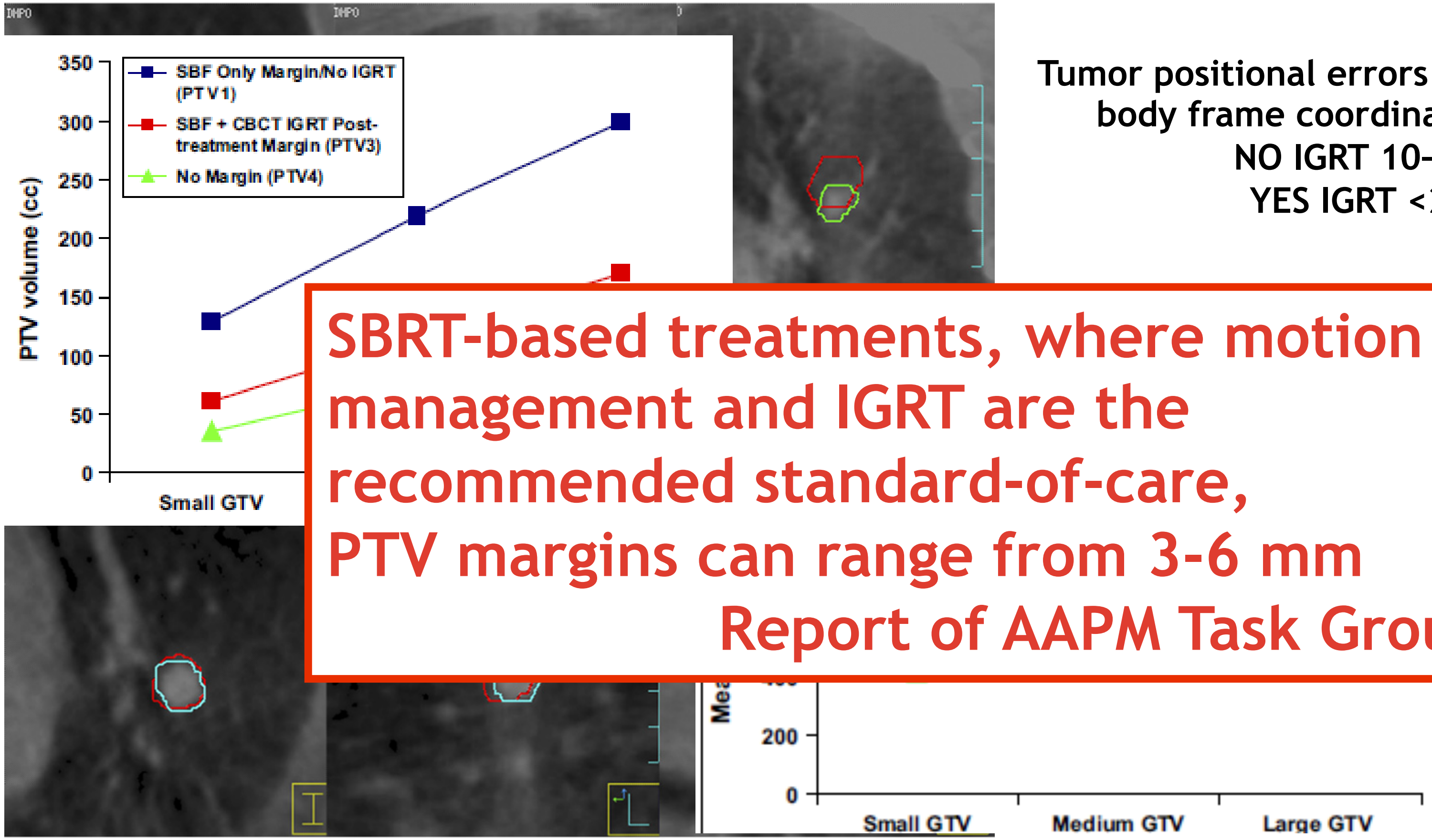
Glide-Hurst CK, J Thorac Dis, 2014

Lung - On-line IGRT

CLINICAL INVESTIGATION Grills IJROBP 2008 Lung

IMAGE-GUIDED RADIOTHERAPY VIA DAILY ONLINE CONE-BEAM CT SUBSTANTIALLY REDUCES MARGIN REQUIREMENTS FOR STEREOTACTIC LUNG RADIOTHERAPY

GTV position pre-correction: Planning CT GTV in Red; Pre-Correction GTV in Green.



Transverse Sagittal Coronal

308 CBCT, 24 pts

Tumor positional errors using stereotactic body frame coordinates for setup :
NO IGRT 10-12mm,
YES IGRT <2 mm.

SBRT-based treatments, where motion management and IGRT are the recommended standard-of-care, PTV margins can range from 3-6 mm

Report of AAPM Task Group

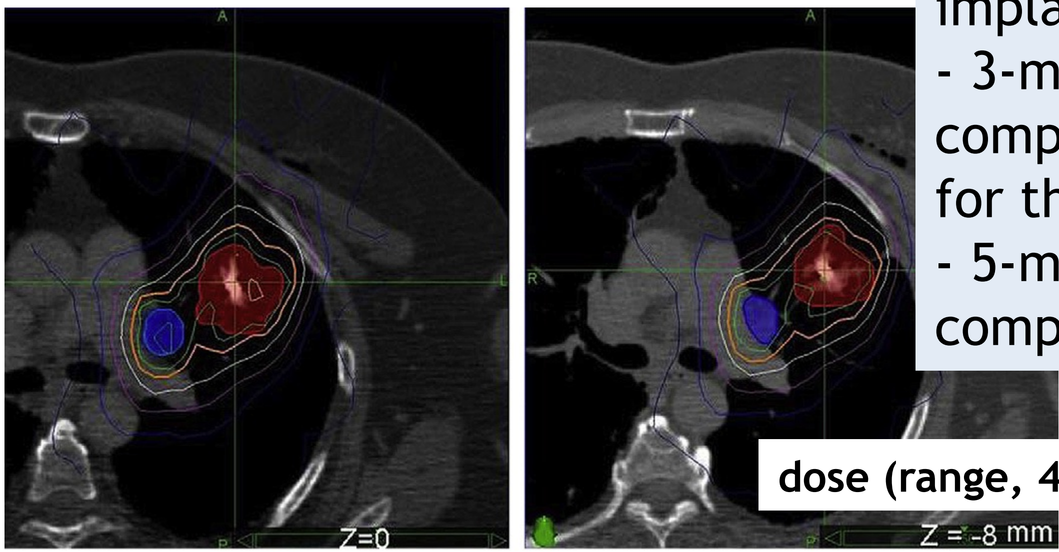
Lung - Tracking

PHYSICS CONTRIBUTION Lu IJROBP 2008

ORGAN DEFORMATION AND DOSE COVERAGE IN ROBOTIC RESPIRATORY-TRACKING RADIOTHERAPY

Respiratory tracking that follows the translational movement of the internal fiducials minimizes the uncertainties in dose delivery.
However, the effect of deformation, defined as any changes in the body and organs relative to the center of fiducials, remains unanswered.
This study investigated this problem and a possible solution.

12 lung lesions.
For lung patients with properly implanted fiducials:
- 3-mm margin is required to compensate
for the deformation
- 5-mm margin is required to compensate for all uncertainties.



dose (range, 48–60 Gy) covered 95% of PTV

(A) (B)

THE BREAST ISSUE

REPORTS OF PRACTICAL ONCOLOGY AND RADIOTHERAPY 16 (2011) 77–81

Detection of setup uncertainties with 3D surface registration system for conformal radiotherapy of breast cancer

Letizia Deantonio[a], Laura Masini[a], Gianfranco Loi[b], Giuseppina Gambaro[a], Cesare Bolchini[a], Marco Krengli[a,c,]*

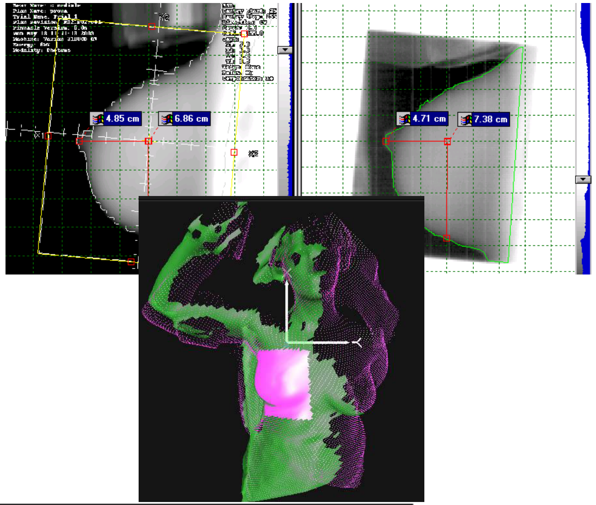


Table 1 – Systematic and random errors cm along vertical and longitudinal axis.

Positioning system	Field axis	Systematic error (mean ± SD)		Random error (mean ± SD)	
EPID	Vertical	0.10 ± 0.08		0.12 ± 0.04	
ALIGNRT	Vertical	0.12 ± 0.26	P> 0,05	0.16 ± 0.06	P> 0,05
EPID	Longitudinal	0.10 ± 013		0.13 ± 0.07	
ALIGNRT	Longitudinal	0.07 ± 0.17		0.18 ± 0.07	

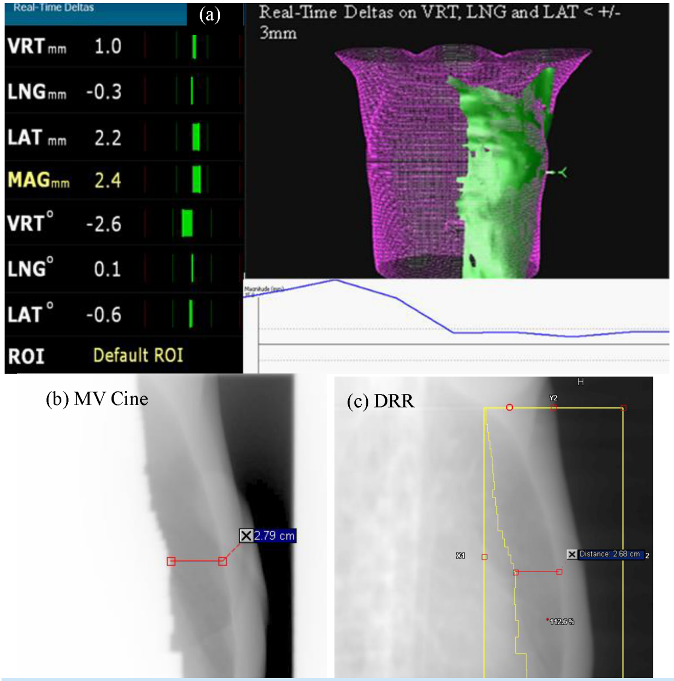
The AlignRT is reliable in detecting setup errors in breast cancer patients to guarantee the reproducibility of patient setup in fractionated RT for breast cancer. It is fast, simple and non invasive. No extra-dose.

FROM THE EPID and SURFACE IMAGING…

THE BREAST ISSUE

…TO THE RESPIRATORY GATING

Improving Intra-Fractional Target Position Accuracy Using a 3D Surface Surrogate for Left Breast Irradiation Using the Respiratory-Gated Deep-Inspiration Breath-Hold Technique Rong et al, PLOS 2014



To evaluate the use of 3D optical surface imaging as a surrogate for respiratory gated deep-inspiration breath hold (DIBH) for left breast irradiation, compared with RPM (real-time position management) gating system. Reduction in heart dose can be achieved using DIBH for left breast radiation.

RPM: inferior correlation with the actual target position; it may not be an adequate surrogate in defining the breath-hold level.
AlignRT : superior correlation with the actual target positioning during DIBH.
.

Conclusion: The RPM system alone may not be sufficient for the required level of accuracy in left-sided breast/CW DIBH treatments. The 3D surface imaging can be used to ensure patient setup and monitor inter- and intra- fractional motions. Furthermore, the target position accuracy during DIBH treatment can be improved by AlignRT as a superior surrogate, in addition to the RPM system.

THE BREAST ISSUE

frontiers in
ONCOLOGY

REVIEW ARTICLE
published: 23 September 2014
doi: 10.3389/fonc.2014.00257

Image-guided radiotherapy for cardiac sparing in patients with left-sided breast cancer

Claire Lemanski[1], Juliette Thariat[2], Federico L. Ampil[3], Satya Bose[4], Jacqueline Vock[5], Rick Davis[6], Alexander Chi[7], Suresh Dutta[8], William Woods[9], Anand Desai[10], Juan Godinez[11], Ulf Karlsson[12], Melissa Mills[13], Nam Phong Nguyen[4]*, Vincent Vinh-Hung[14] and The International Geriatric Radiotherapy Group

[1] *Department of Radiation Oncology, Centre Val d'Aurelle, Montpellier, France*
[2] *Department of Radiation Oncology, University of Nice, Nice, France*
[3] *Department of Radiation Oncology, Louisiana State University, Shreveport, LA, USA*
[4] *Department of Radiation Oncology, Howard University, Washington, DC, USA*
[5] *Department of Radiation Oncology, Lindenhofspital, Bern, Switzerland*
[6] *Michael D. Watchtel Cancer Center, Oshkosh, WI, USA*
[7] *Department of Radiation Oncology, University of West Virginia, Morgantown, WV, USA*
[8] *Department of Radiation Oncology, Medicine and Radiation Oncology PA, San Antonio, TX, USA*
[9] *Department of Radiation Oncology, Richard A. Henson Institute, Salisbury, MD, USA*
[10] *Department of Radiation Oncology, Akron City Hospital, Akron, OH, USA*
[11] *Florida Radiation Oncology Group, Department of Radiation Oncology, Jacksonville, FL, USA*
[12] *Department of Radiation Oncology, Marshfield Clinic, Marshfield, WI, USA*
[13] *Department of Radiation Oncology, University of Arizona, Tucson, AZ, USA*
[14] *Department of Radiation Oncology, University of Martinique Hospital, Martinique, France*

Edited by:
John Varlotto, University of Massachusetts Medical Center, USA

Reviewed by:
John E. Mignano, Tufts Medical Center, USA
Heloisa De Andrade Carvalho, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, Brazil

****Correspondence:***
Nam Phong Nguyen, Howard University, 2041 Georgia Avenue NW, Washington, DC 20060, USA
e-mail: namphong.nguyen@yahoo.com

Patients with left-sided breast cancer are at risk of cardiac toxicity because of cardiac irradiation during radiotherapy with the conventional 3-dimensional conformal radiotherapy technique. In addition, many patients may receive chemotherapy prior to radiation, which may damage the myocardium and may increase the potential for late cardiac complications. New radiotherapy techniques such as intensity-modulated radiotherapy (IMRT) may decrease the risk of cardiac toxicity because of the steep dose gradient limiting the volume of the heart irradiated to a high dose. Image-guided radiotherapy (IGRT) is a new technique of IMRT delivery with daily imaging, which may further reduce excessive cardiac irradiation. Preliminary results of IGRT for cardiac sparing in patients with left-sided breast cancer are promising and need to be investigated in future prospective clinical studies.

Keywords: breast cancer, left breast, cardiac toxicity, IGRT

THE LIVER ISSUE

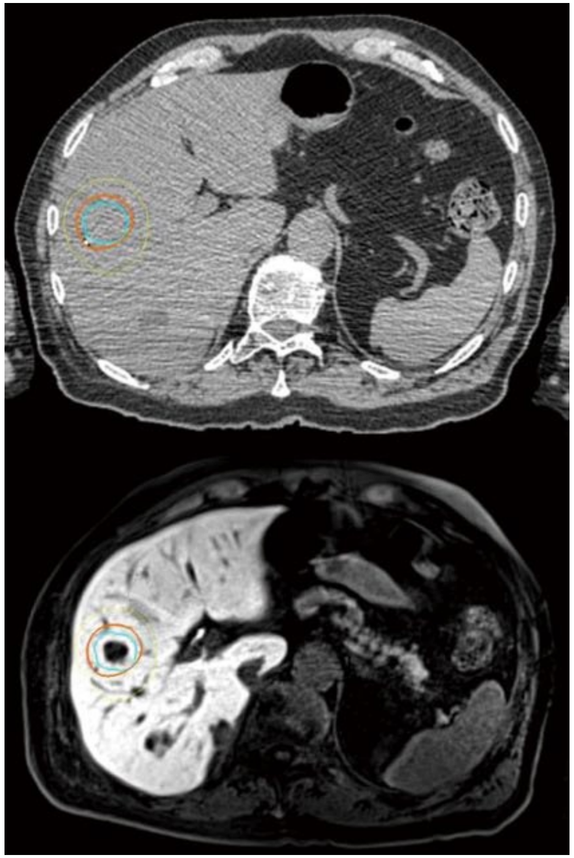
The relatively low tolerance of the whole liver (20-30 Gy in 2-3 Gy per fraction) is a limiting factor (radiation induced liver disease - RILD) for high dose RT (SBRT).

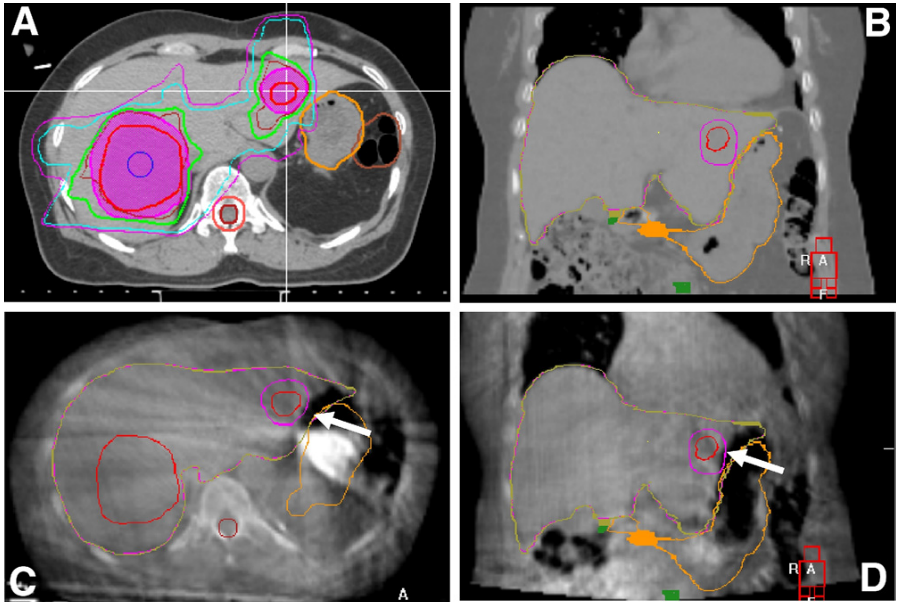
Ref.	Design	No of patients	Tumor size	SABR dose	Toxicity	Outcomes
Scorsetti *et al*[15]	Phase II (preliminary report)	61 (76 tumors)	1.8-134.3 cm^3 (mean 18.6 cm^3)	75 Gy in 3 fractions	No case of RILD. Twenty-six percent had grade 2 transaminase increase (normalised in 3 mo). Grade 2 fatigue in 65% patients, one grade 3 chest wall pain which regressed within 1 year.	1-yr LC94, 22-mo LC 90.6%
Goodman *et al*[16]	Phase I (HCC and liver mets)	26 (19 liver mets)	0.8-146.6 mL (median, 32.6 mL)	Dose escalation, 18-30 Gy (1 fr)	No dose-limiting toxicity 4 cases of Grade 2 late toxicity (2 GI, 2 soft tissue/rib)	1-yr local failure, 3% 2-yr OS, 49% (mets only)
Ambrosino *et al*[17]	Prospective cohort	27	20-165 mL (median, 69 mL)	25-60 Gy (3 fr)	No serious toxicity	Crude LC rate 74%
Lee *et al*[18]	Phase I - II	68	1.2-3090 mL (median, 75.9 mL)	Individualized dose, 27.7-60 Gy (6 fr)	No RILD, 10% Grade 3/4 acute toxicity No Grade 3/4 late toxicity	1-yr LC, 71% Median survival, 17.6 mo
Rusthoven *et al*[19]	Phase I - II	47	0.75-97.98 mL (median, 14.93 mL)	Dose escalation, 36-60 Gy (3 fr)	No RILD, Late Grade ¾ < 2%	1-yr LC, 95% 2-yr LC, 92% Median survival, 20.5 mo
Høyer *et al*[10]	Phase II (CRC oligomets)	64 (44 liver mets)	1-8.8 cm (median, 3.5 cm)	45 Gy (3 fr)	One liver failure, two severe late GI Toxicities	2-yr LC, 79% (by tumor) and 64% (by patient)
Méndez Romero *et al*[20]	Phase I - II (HCC and mets)	25 (17 liver mets)	1.1-322 mL (median, 22.2 mL)	30-37.5 Gy (3 fr)	Two Grade 3 liver toxicities	2-yr LC, 86% 2-yr OS, 62%
Herfarth *et al*[21]	Phase I - II	35	1-132 mL (median, 10 mL)	Dose escalation, 14-26 Gy (1 fr)	No significant toxicity reported	1-yr LC, 71% 18-mo LC, 67% 1-yr OS, 72%

Nair et al, WJR 2014

THE LIVER ISSUE

PTV:
5 mm radial margin
10 mm cranio-caudal margin.
5 mm or less in case of fiducial based guidance





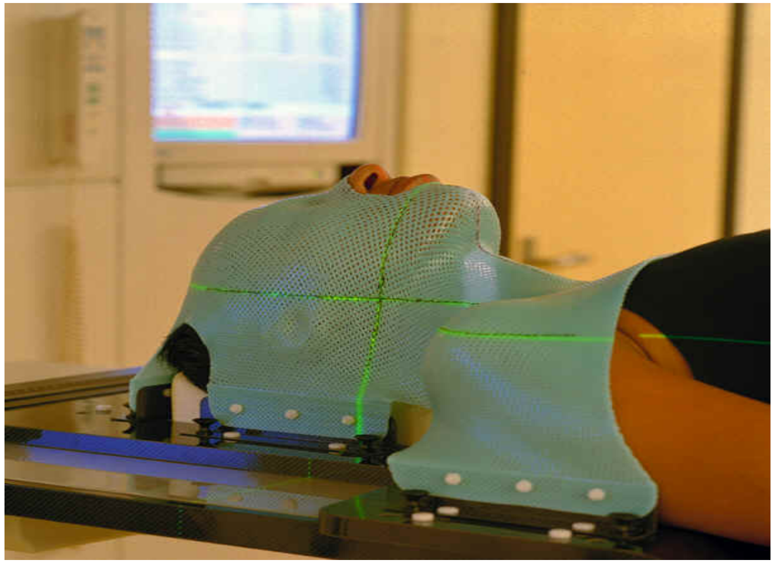
3rd fraction CBCT scans: a random change in gastric filling pushed the left lobe medially, whereas the right lobe alignment was acceptable. Without replanning :

- the dose to the stomach higher than acceptable
- the left lobe tumor underdosed

Nair et al, WJR Review 2014

The H&N ISSUE

The proximity of targets to critical structures require high-dose gradients.
Radiation techniques have then mandated more accuracy and reliability.
It is a matter of “how much” rather than “if”
IGRT is needed.



Thermoplastic mask immobilization and weekly 2-dimensional imaging with bone matching is typically used with PTV margins of 3-5 mm.
No direct impact of more intense IGRT has been shown, but a 50% reduction of PTV margins has been obtained when using daily CBCT scanning.

Den et al, IJROBP 2010
Buyold A et al, Semin Radiat Oncol 2012

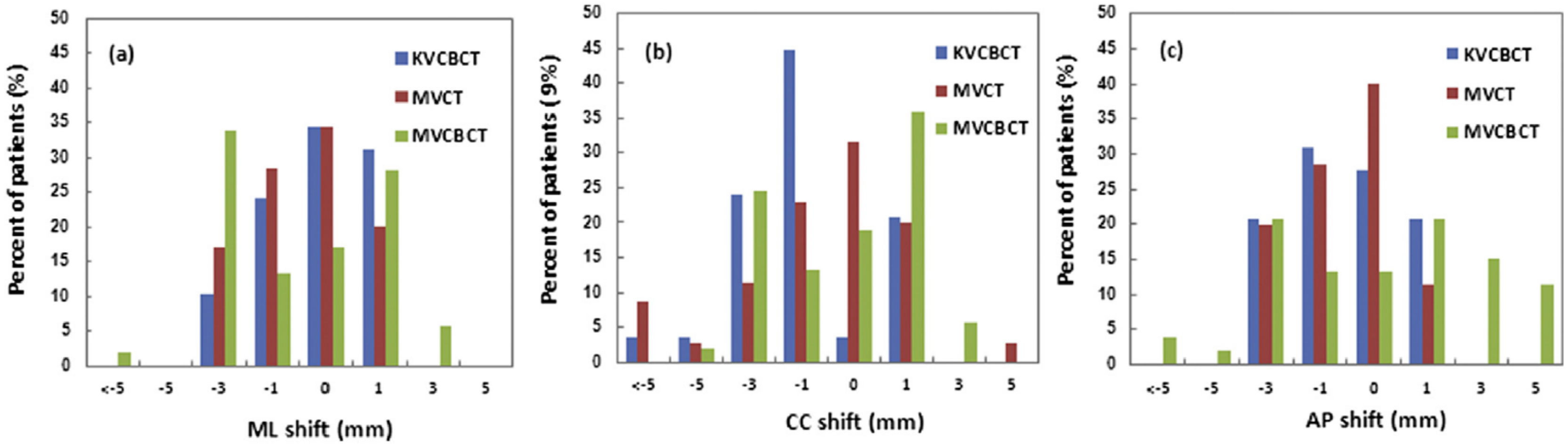
The H&N ISSUE

Physics Contribution

Sharon Qi et al, IJROBP 2013

Assessment of Interfraction Patient Setup for Head-and-Neck Cancer Intensity Modulated Radiation Therapy Using Multiple Computed Tomography-Based Image Guidance

To assess interfraction patient setup variations for 3 CT-based on-board IGRT modalities (MVCBCT-kVCBCT-MVFBCT):



>3300 CT scans

Conclusions: Daily random setup errors and CTV-to-PTV margins for treatment of head-and-neck cancer were affected by imaging quality. Our data indicated that larger margins were associated with MVFBCT and MVCBCT, compared with smaller margins for KVCBCT. IGRT modalities with better image quality are encouraged in clinical practice.

THE PROSTATE ISSUE

Clinical Investigation: Genitourinary Cancer Zelefsky et al, IJROBP 2012

Improved Clinical Outcomes With High-Dose Image Guided Radiotherapy Compared With Non-IGRT for the Treatment of Clinically Localized Prostate Cancer

Purpose: To compare toxicity profiles and biochemical tumor control outcomes between patients treated with high–dose image-guided radiotherapy (IGRT) and high–dose intensity-modulated radiotherapy (IMRT) for clinically localized prostate cancer.

Materials and Methods: Between 2008 and 2009, 186 patients with prostate cancer were treated with IGRT to a dose of 86.4 Gy with daily correction of the target position based on kilovoltage imaging of implanted prostatic fiducial markers. This group of patients was retrospectively compared with a similar cohort of 190 patients who were treated between 2006 and 2007 with IMRT to the same prescription dose without, however, implanted fiducial markers in place (non-IGRT). The median follow-up time was 2.8 years (range, 2–6 years).

Significant reduction of G2 GU toxicity
For high-risk patients, a significant improvement was observed at 3 years for patients treated with IGRT compared with non-IGRT.

THE PROSTATE ISSUE

Mayyas et al, Med Phys 2013

Evaluation of multiple image-based modalities for image-guided radiation therapy (IGRT) of prostate carcinoma: A prospective study

Purpose: Setup e uncertainty
in prostate cancer ies 3D ultra-
sound (US), kV nted electro-
magnetic transpo rrors during
intensity-modulat

Interfraction shifts evaluated prospectively on a protocol of 1100 fractions for prostate cancer, and imaged daily :
kV x rays, CBCT, 3D ultrasound, and electromagnetic transponders, yielded similar results, planning margins on the order of 10–11 mm to account for setup errors based on skin tattoo alignment.
Image guidance was found to reduce these setup error margins to less than 4 mm.

ferent imaging modalities.

		L/R		
	US	CBCT	kV	US
.4	– 1.4	1.1	0.5	0.0
.1	3.5	2.4	2.6	2.8
.0	3.8	2.5	2.4	3.6

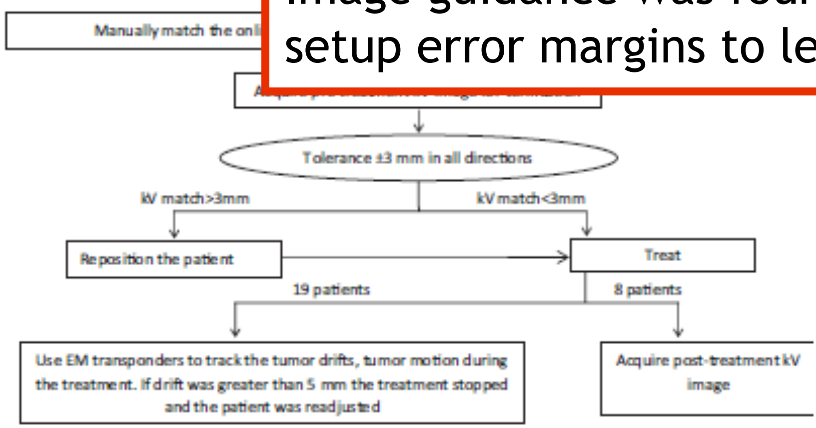


TABLE VII. Margin estimation for interfraction shifts for CBCT, kV, and US imaging modalities, based on the initial, skin-mark-based alignment. Results are averaged over 27 patients.

	A/P			S/I			L/R		
	CBCT	kV	US	CBCT	kV	US	CBCT	kV	US
M (mm)	9.7	10.5	11.1	8.3	11.2	11.4	7.8	8.2	9.5

Radiation Oncology

BioMed Central

Research

Open Access

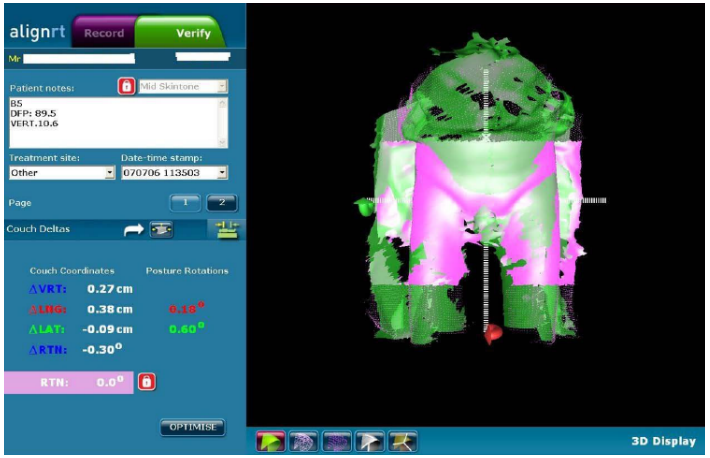
Reproducibility of patient setup by surface image registration system in conformal radiotherapy of prostate cancer

Marco Krengli*[1,2], Simone Gaiano[1], Eleonora Mones[3], Andrea Ballarè[1], Debora Beldì[1], Cesare Bolchini[1] and Gianfranco Loi[3]

Radiation Oncology 2009, 4:9

Table 1: Systematic and random errors (mm) along the three main axes (X, Y, and Z) detected by AlignRT

Axis	Systematic error (mean ± SD)	Random error (mean ± SD)
X	1.2 ± 2.3	0.3 ± 2.9
Y	0.0 ± 1.4	0.5 ± 2.0
Z	2.0 ± 1.8	-0.7 ± 2.4



Correlation factors calculated by linear regression analysis between the errors measured by AlignRT and EPID ranged from 0.77 to 0.92 with a mean of 0.85 and SD of 0.13. The setup errors measured by Alignrt are highly reproducible and correlate with the setup errors detected by EPID.

THE PROSTATE ISSUE

US & SURFACE IMAGING MATCHING

Clarity ® - Resonant Medical, Montreal, CA

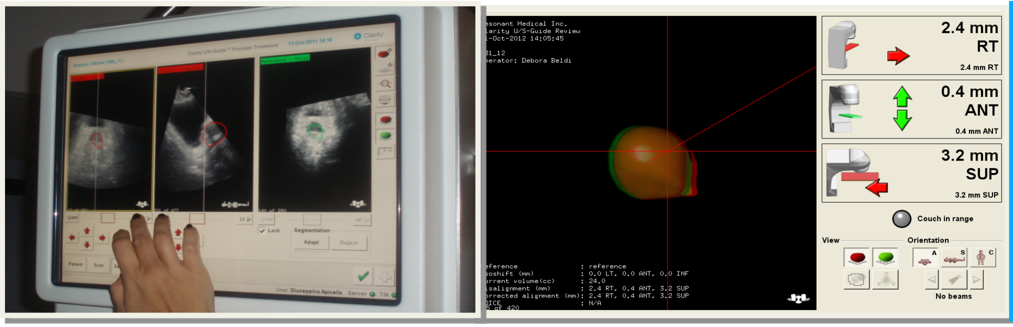
Align-RT®-VisionRT, London, UK

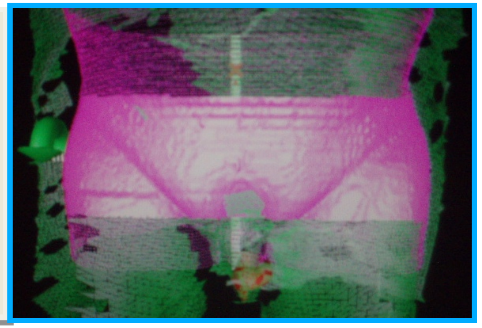
Analysis of the correlations between interfractions variations of US and surface imaging.

36 pts with prostate cancer treatde by IMRT 76-78 Gy

Daily IGRT with AlignRT and Ultrasound

1179 images





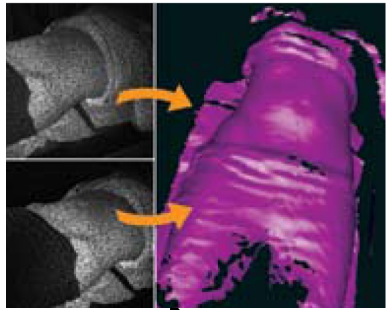
No correlation was found in the 3 spatial directions (x, y, z) between Clarity ed AlignRT.

Align-RT → Set-up error

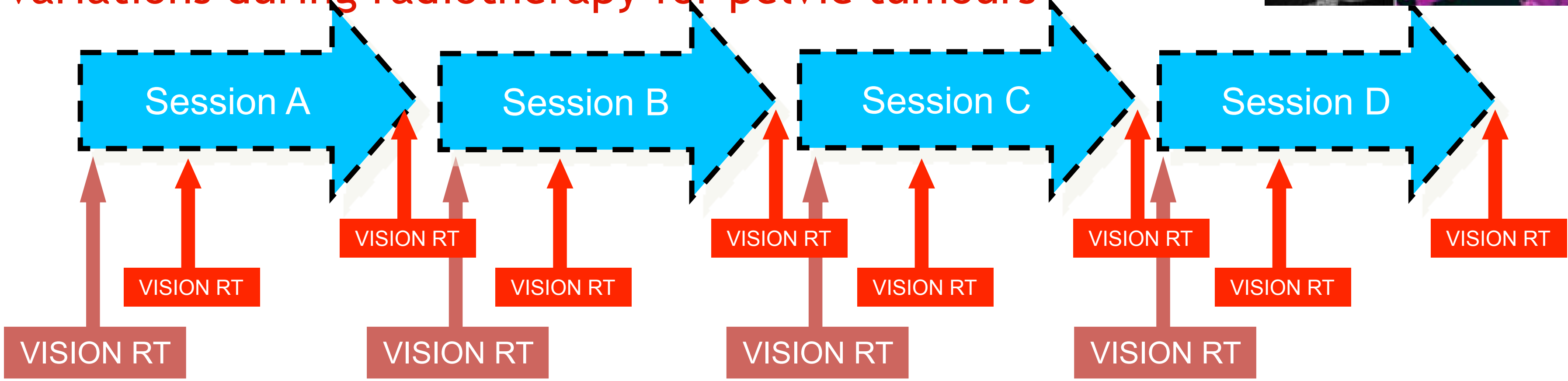
US → Organ motion

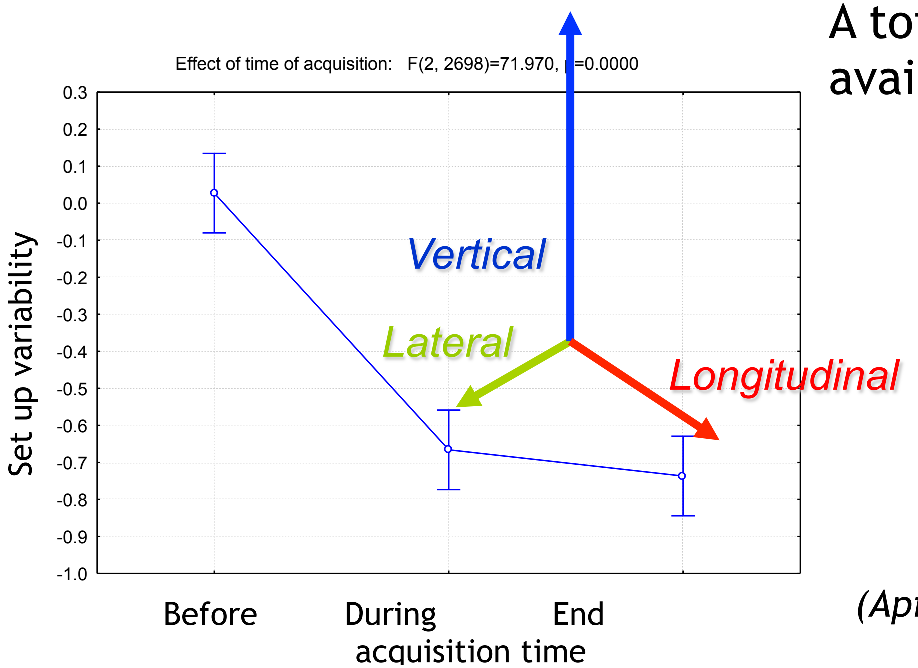
(Krengli M et al, Proc. ESTRO 33, Radiother Oncol, 2014)

THE PROSTATE ISSUE



3D surface imaging for detection of intrafraction setup variations during radiotherapy for pelvic tumours





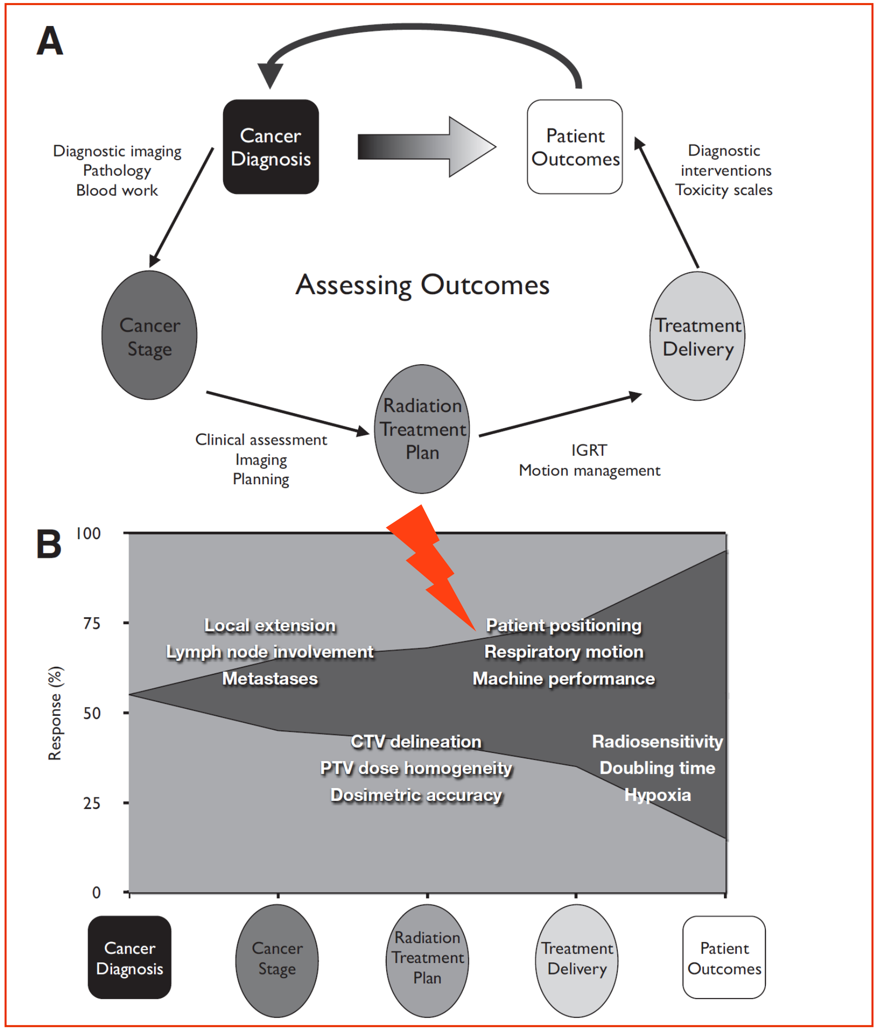
A total of 2605 images from 317 fractions were available for evaluation.

The largest displacement of patients occurred during the very first minutes of treatment session, with a maximum misalignment of 0.4 mm in the vertical direction between the starting and mid-treatment acquisition

(Apicella G et al, Proc. ESTRO 33, Radiother Oncol, 2014)

CONCLUSIONS I

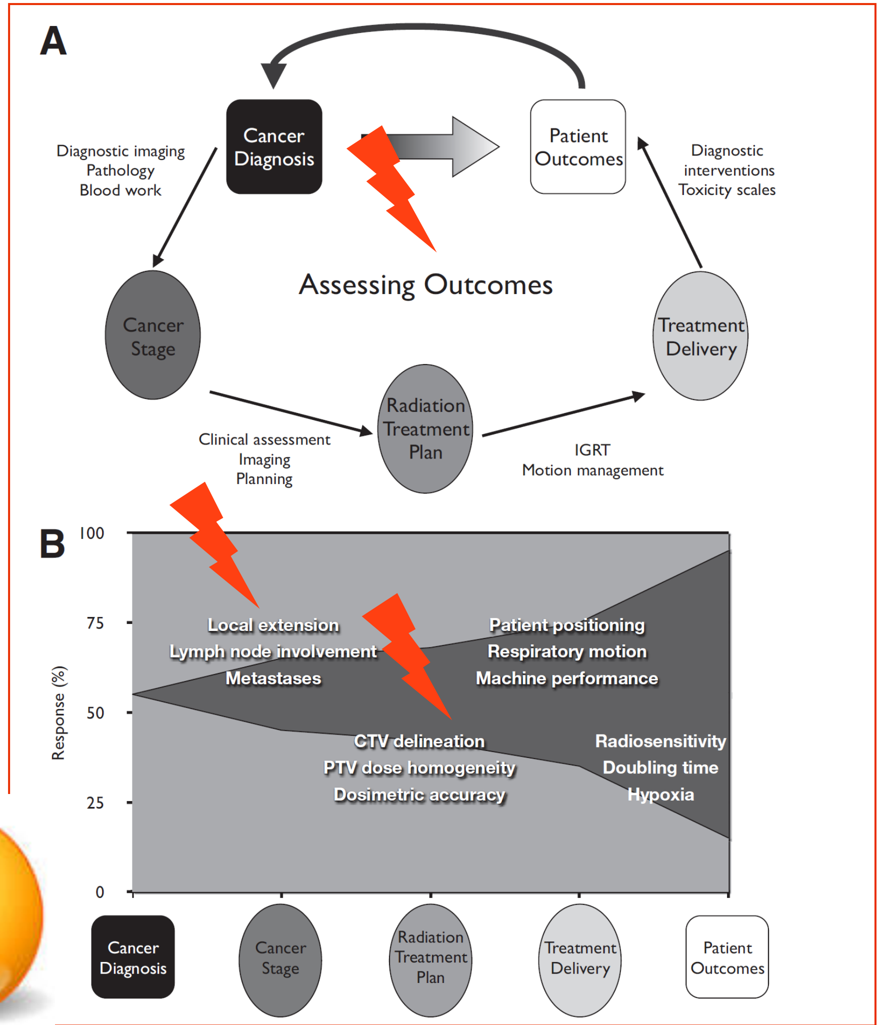
- IGRT is currently a solid tool to tackle the problem of radiotherapy accuracy.
- State-of-the-art IGRT can reduce positioning uncertainty to the extent that a 1- to 2-mm PTV margin would often be sufficient.
- IGRT can be used as a quality assurance tool itself.
- IGRT has been shown to facilitate implementation of new RT techniques (eg, liver and lung SBRT) and in selected sites (prostate) can reduce toxicity and improve local control.



CONCLUSIONS II

- The whole chain of interventions in the RT process should be prospectively assessed.
- This is particularly important because other steps in the RT process :
    - natural history of the disease
    - contouring
    - valid measurements of toxicity

are at least as important as high geometric precision.



AND REMEMBER
THE BRAIN GUIDED
RADIOTHERAPY