I SESSIONE

Radioterapia e carcinoma mammario

Radioterapia: ruolo delle tecnologie avanzate per ridurre la tossicità

Rosario Mazzola
Dipartimento di Radioterapia Oncologica Avanzata
IRCCS Sacro Cuore Don Calabria
Negrar di Valpolicella

I NUMERI DEL CANCRO IN ITALIA 2022

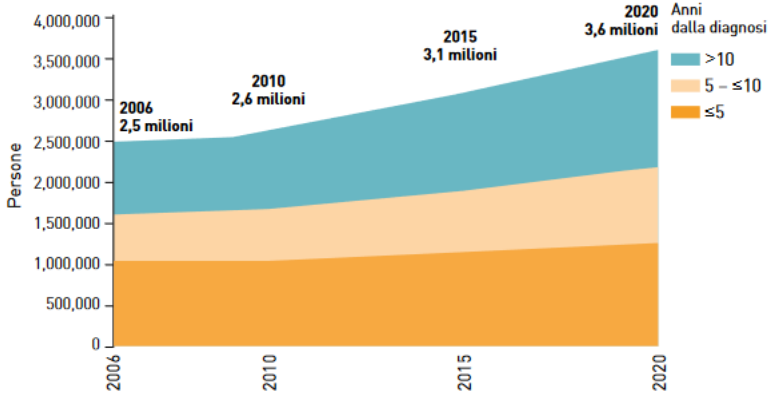

FIGURA 4. Numero di persone che vivono dopo una diagnosi di tumore per tempo dalla diagnosi

Fonte: Modificata da Guzzinati et al 2018

MAMMELLA	
Incidenza	Nel 2022, sono state stimate circa 55.700 nuove diagnosi nelle donne
Mortalità	Nel 2021, sono stimati 12.500 decessi. Le stime per il 2022 non sono disponibili
Sopravvivenza netta a 5 anni dalla diagnosi	88%
Probabilità di vivere ulteriori 4 anni condizionata ad aver superato il primo anno dopo la diagnosi	91%
Prevalenza	Sono 834.200 le donne viventi in Italia dopo una diagnosi di tumore della mammella

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Foundations for a modern Precision Radiation Oncology

The Balistic point of view…

The Strategic point of view…

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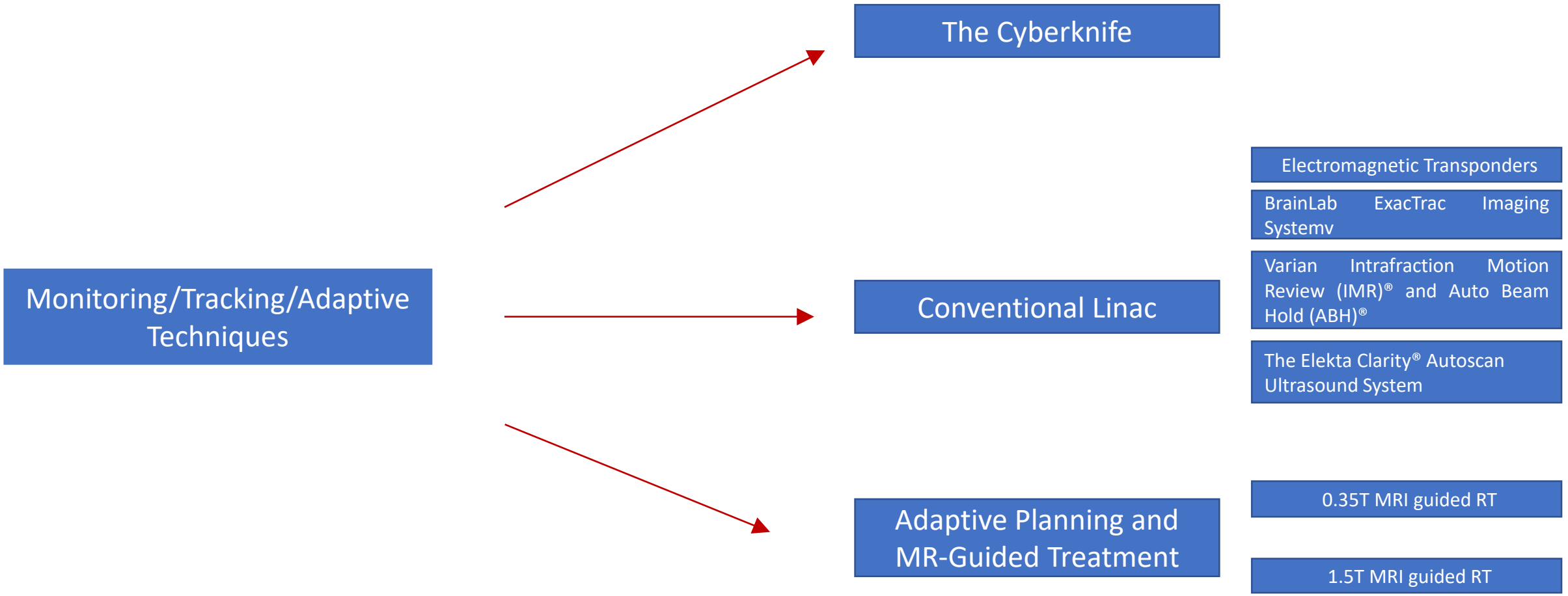
How technology could optimize clinical outcomes in Radiation Oncology?

Real-time tracking and adaptive treatments with different technologies



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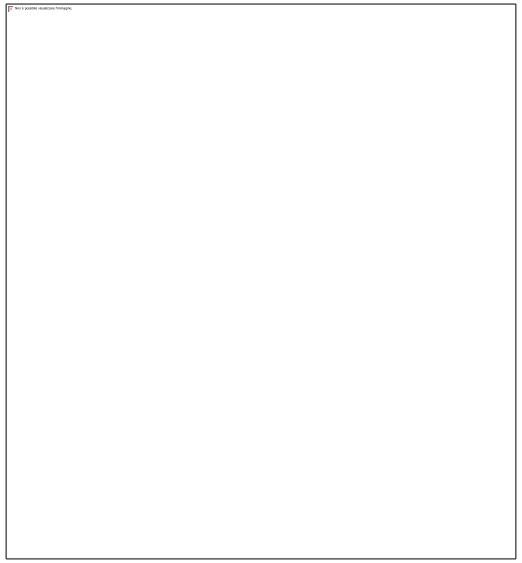
RADIATION-INDUCED HEART DISEASE
Lessons from the past in the era of “modern” radiation therapy

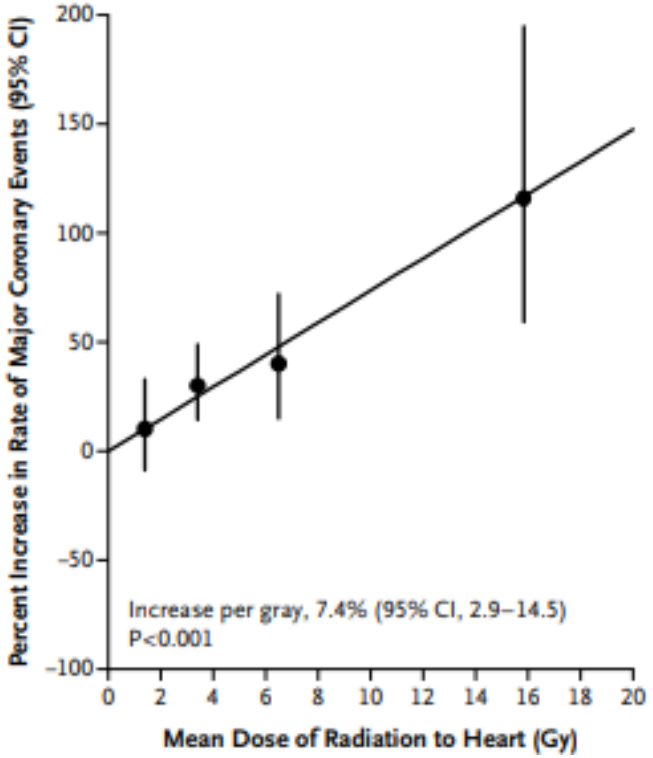
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 MARCH 14, 2013 VOL. 368 NO. 11

Risk of Ischemic Heart Disease in Women after Radiotherapy for Breast Cancer

Sarah C. Darby, Ph.D., Marianne Ewertz, D.M.Sc., Paul McGale, Ph.D., Anna M. Bennet, Ph.D., Ulla Blom-Goldman, M.D., Dorthe Brønnum, R.N., Candace Correa, M.D., David Cutter, F.R.C.R., Giovanna Gagliardi, Ph.D., Bruna Gigante, Ph.D., Maj-Britt Jensen, M.Sc., Andrew Nisbet, Ph.D., Richard Peto, F.R.S., Kazem Rahimi, D.M., Carolyn Taylor, D.Phil., and Per Hall, Ph.D.





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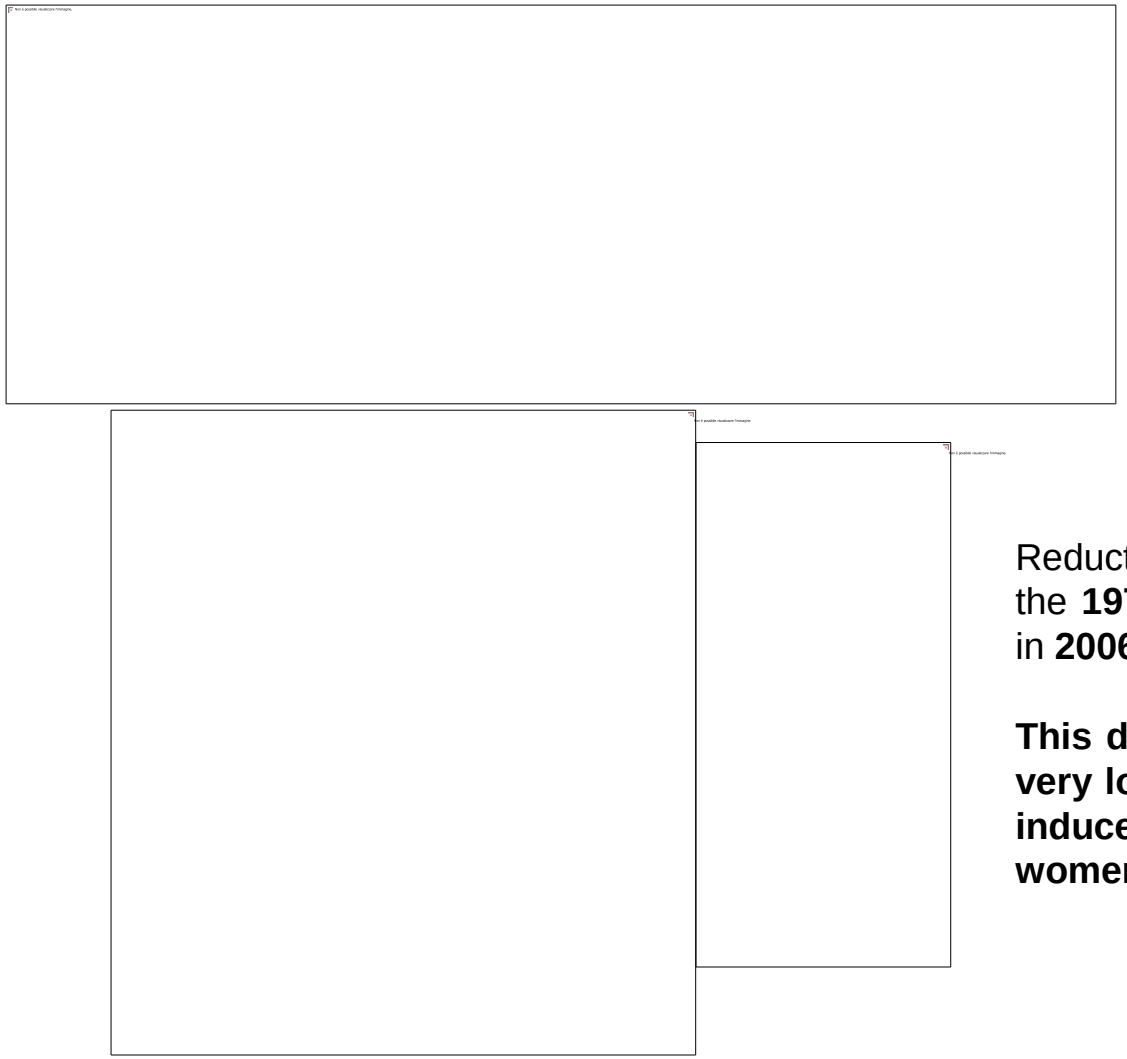
Lessons from the past in the era of “modern” radiation therapy



Reductions in mean heart dose from **13.3Gy** in the **1970s,** to **4.7Gy** in the **1990s,** and **2.3Gy** in **2006**

This decrease seems to have resulted in a very low risk of death caused by radiation-induced heart disease (RIHD), at least for women without cardiac risk factors

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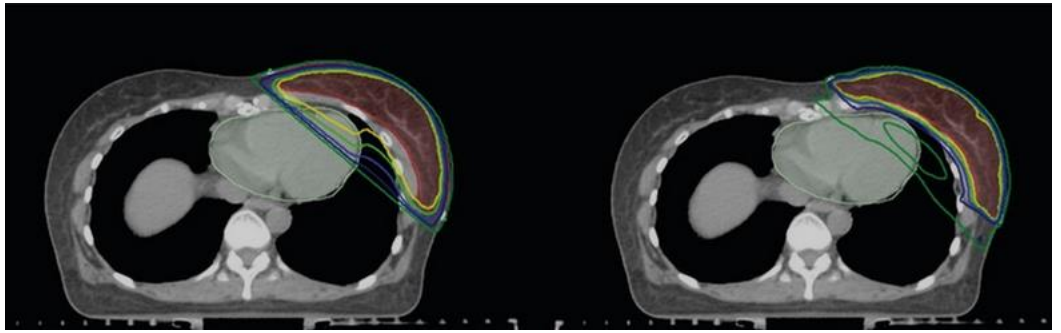
RADIATION-INDUCED HEART DISEASE
Lessons from the past in the era of “modern” radiation therapy

Radiol med
DOI 10.1007/s11547-016-0700-z

RADIOTHERAPY

Three-dimensional conformal versus intensity modulated radiotherapy in breast cancer treatment: is necessary a medical reversal?

Alba Fiorentino[1] · Ruggero Ruggieri[1] · Niccolò Giaj-Levra[1] · Gianluisa Sicignano[1] · Gioacchino Di Paola[2] · Stefania Naccarato[1] · Sergio Fersino[1] · Rosario Mazzola[1] · Umberto Tebano[1,3] · Francesco Ricchetti[1] · Filippo Alongi[1]



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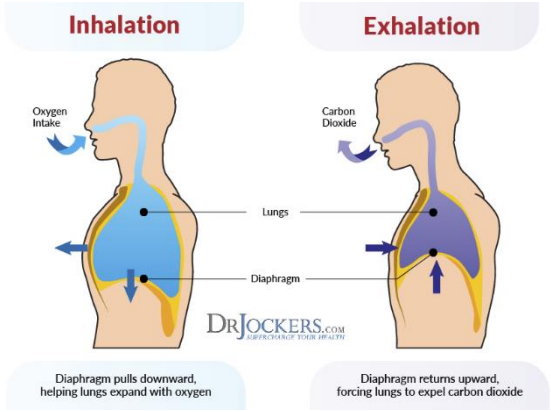
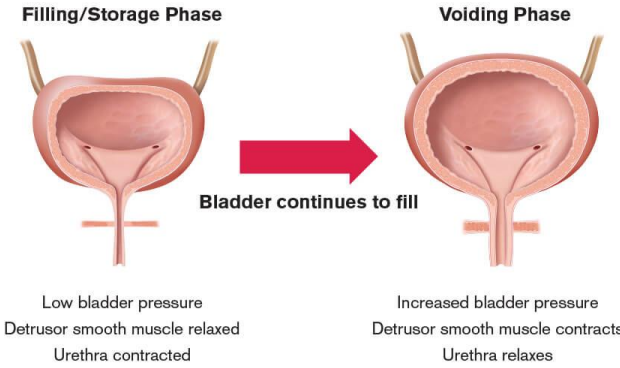
THE PRECISION RT ERA:
MOTION UNCERTANTIES

- ✓ **Intrafraction localization uncertainty** can arise during radiation delivery due to **patient movement** or from internal anatomical motion **through physiological processes such as breathing**.



- ✓ Interfraction localization uncertainty can be created by variations in **patient position or posture**, changes in **target size or shape**, and normal physiological variability such as **bladder and bowel filling**.



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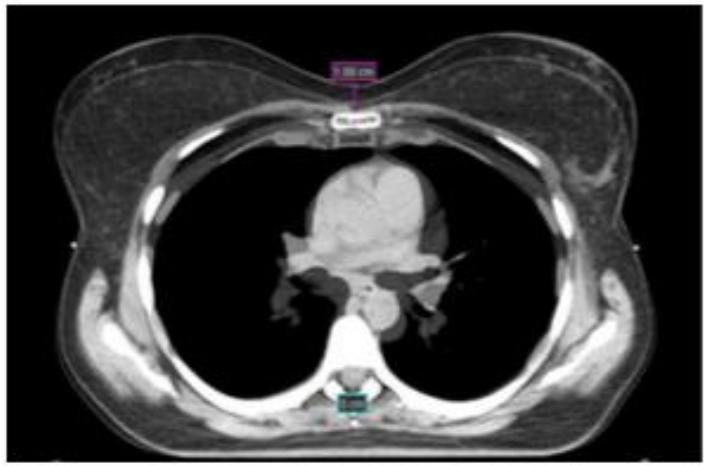
Hoisak et al, Seminars in Radiat Oncol 2018

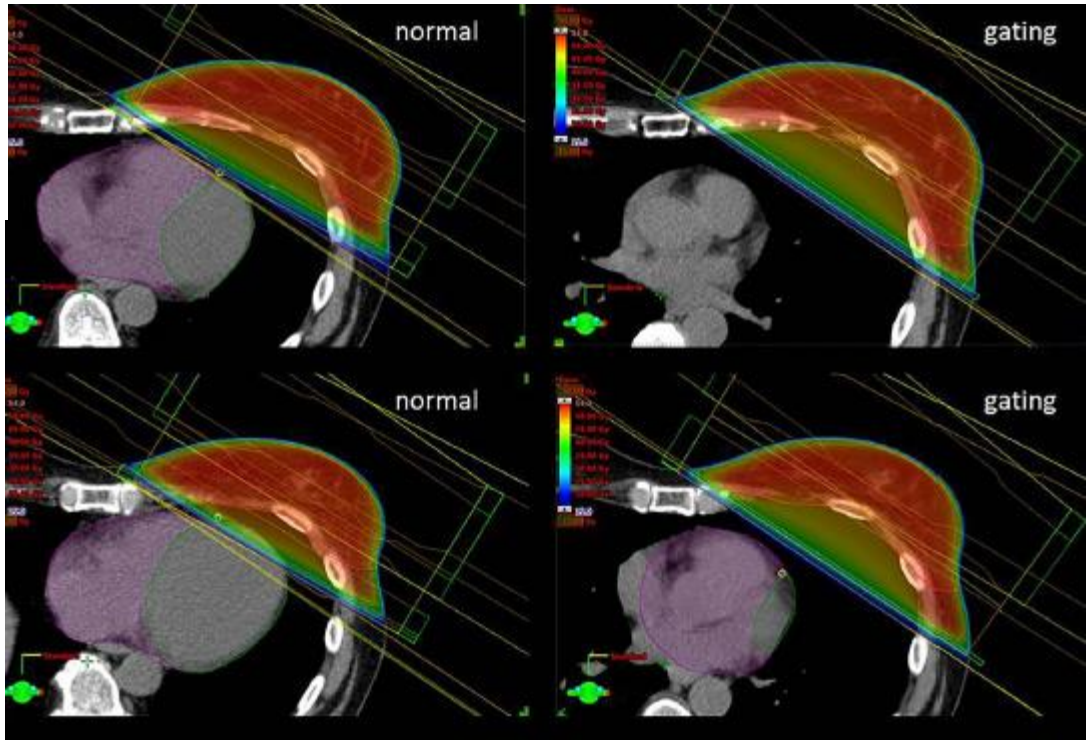
RADIATION-INDUCED HEART DISEASE
Lessons from the past in the era of “modern” radiation therapy



TC-SIM Breath-Hold

> 1 cm

TC-SIM Free-Breathing



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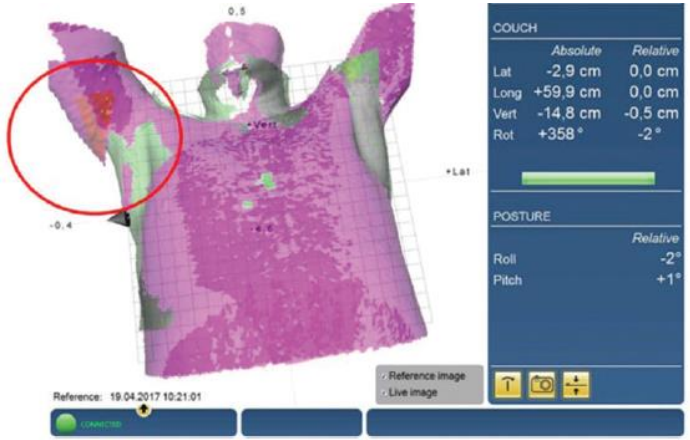
A CONTINUOUS RT IMPROVEMENT:
Surface-Guided-RT

- ✓ Surface-based systems enable a continuous and touchless optical surface scanning of the patients' external surfaces (3D) and are a helpful tool for accurate patient positioning in 6 degrees of freedom without any additional radiation exposure.

- ✓ Furthermore, many commercial systems offer other features, including visual user assistance in the identification of:

- positioning deviations,
- intrafractional motion control,
- automated respiratory gating, especially in the context of deep inspiration breath hold



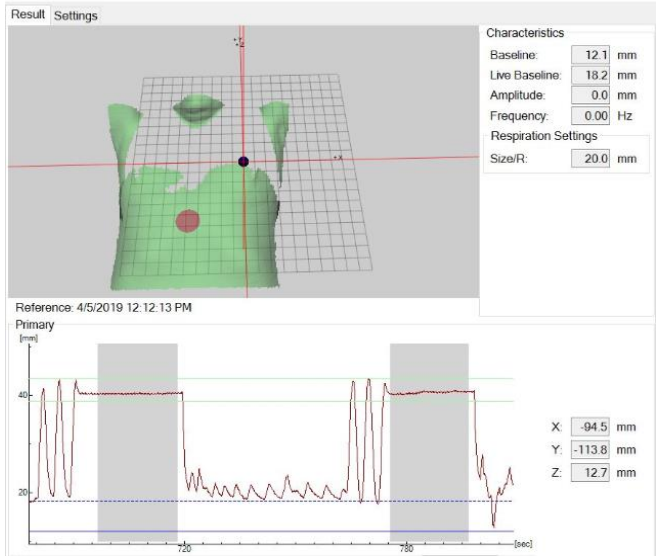
Carl et al, Tech Cancer Res Treat 2018

SIGRT CLINICAL IMPLEMENTATION:
FIRST BREAST DIBH

Patient 68 ys, F, Left Breast Ductal Invasive Carcinoma
Stage IA, post-BCS + SNB

SENTINEL™ 4DCT

Free Breathing and
DIBH CT simulation
Scans

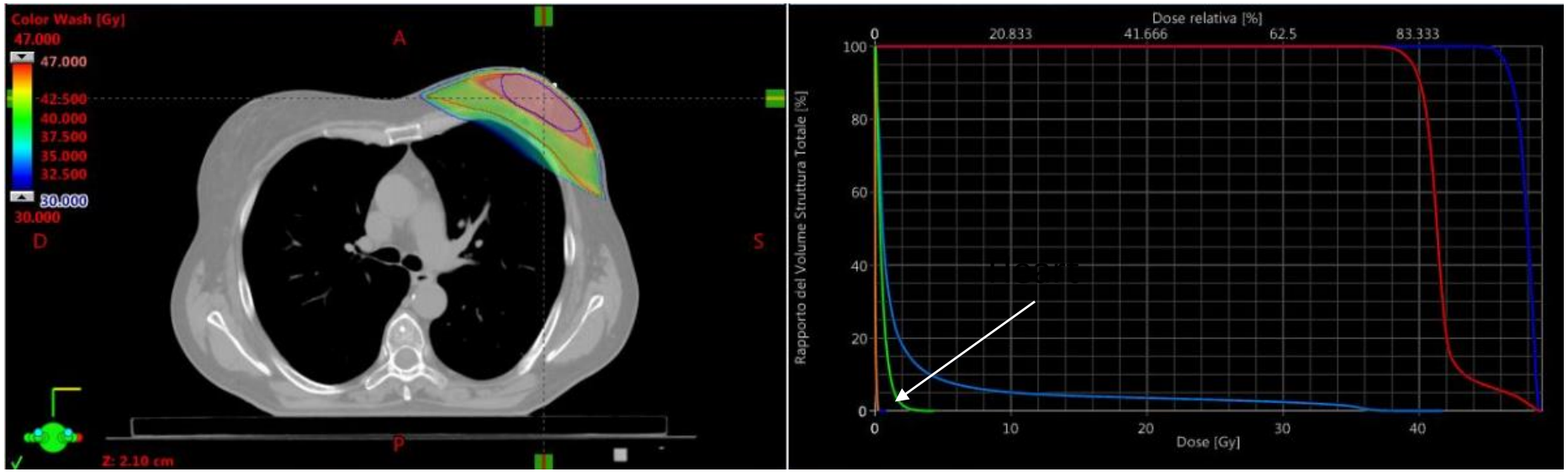


DIBH CT scan acquisition

ADVANCED RADIATION ONCOLOGY DEPARTMENT

SIGRT CLINICAL IMPLEMENTATION:
FIRST BREAST DIBH

Patient 68 ys, F, Left Breast Ductal Invasive Carcinoma
Stage IA, post-BCS + SNB

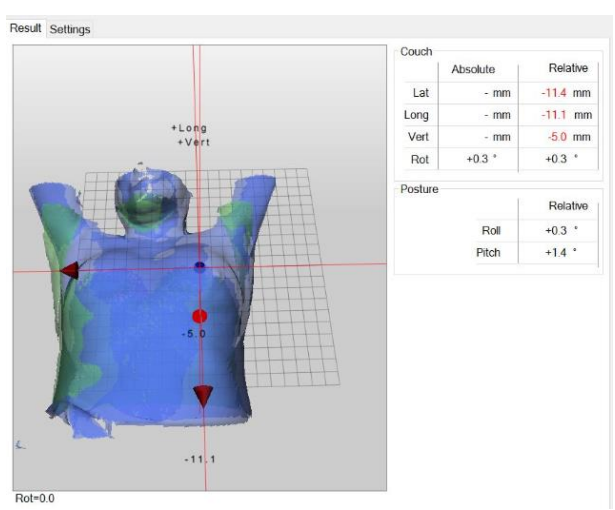


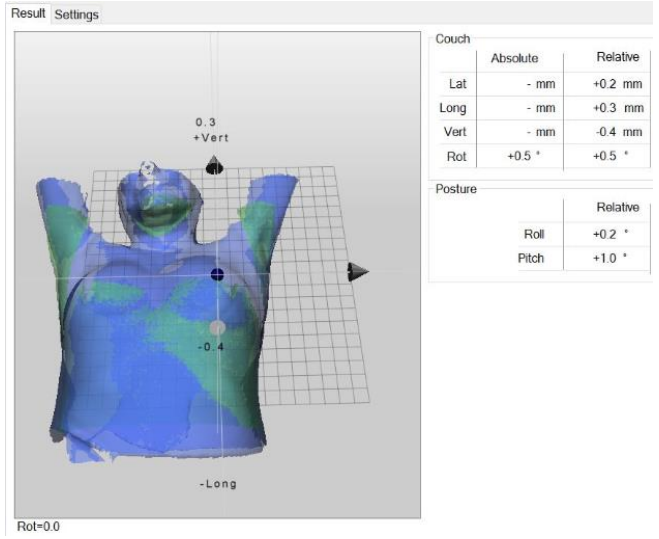
Treatment Planning

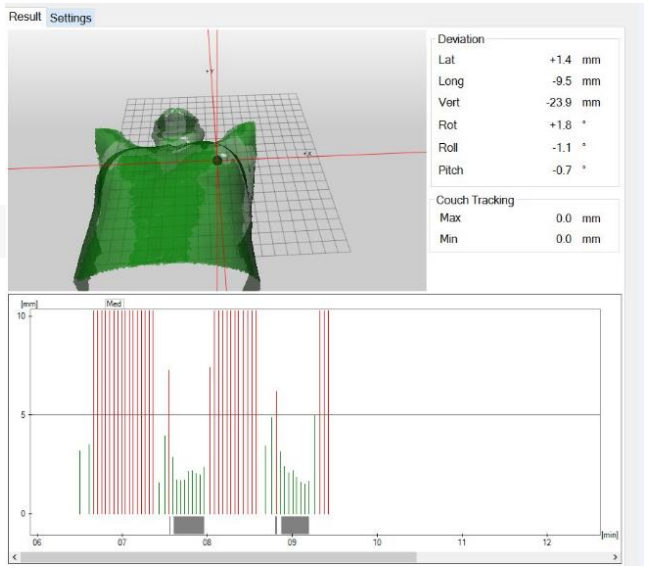
- IMRT plan on True Beam
- Whole Left Breast: Dose 40,5 Gy/15 fx;
- Simultaneous Integrated Boost: Dose 48 Gy/15 fx.

SIGRT CLINICAL IMPLEMENTATION:
FIRST BREAST DIBH

TPositioning and Treatment







Daily Reference acquisition on Linac

Daily Reference Acquisition Matched with Simulation Reference Image

Beam Delivery Treatment during Breath Hold

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SIGRT CLINICAL IMPLEMENTATION:
FIRST BREAST DIBH

Strahlenther Onkol
https://doi.org/10.1007/s00066-018-1350-y

ORIGINAL ARTICLE

Dose variability in different lymph node levels during locoregional breast cancer irradiation: the impact of deep-inspiration breath hold

Montserrat Pazos[1] · Alba Fiorentino[2] · Aurélie Gaasch[1] · Stephan Schönecker[1] · Daniel Reitz[1] · Christian Heinz[1] · Maximilian Niyazi[1] · Marciana-Nona Duma[3] · Filippo Alongi[2,4] · Claus Belka[1] · Stefanie Corradini[1]

Received: 30 April 2018 / Accepted: 10 August 2018

Conclusion A significant movement of the axillary lymph node levels was observed during DIBH in anterior and cranial directions for node-positive breast cancer patients in comparison to FB. The movement leads to a significant dose reduction in level I and level II.

POTENTIAL ROLE OF CATALYST HD TO FOLLOW PATIENTS ALIGNEMENTS

AND MANAGE BREAST+/-REGIONAL DURING DIBH

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Pazos et al, Stralenther Onkol 2018

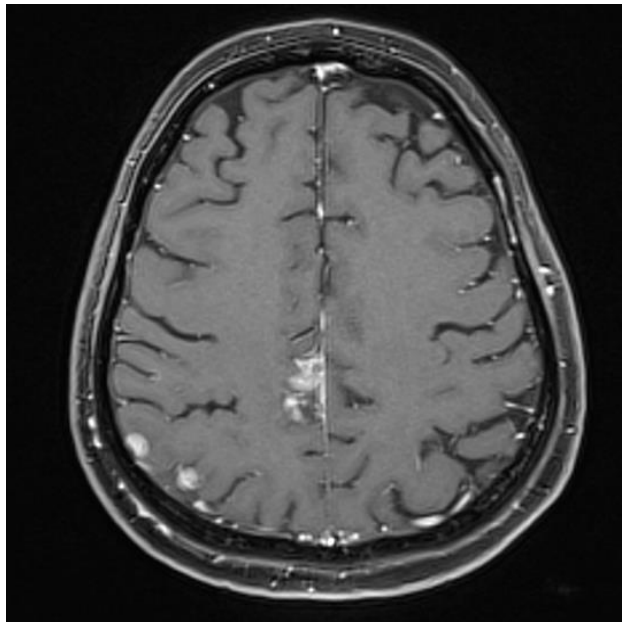
Ruolo delle tecnologie avanzate per ridurre la tossicità nella fase metastatica?

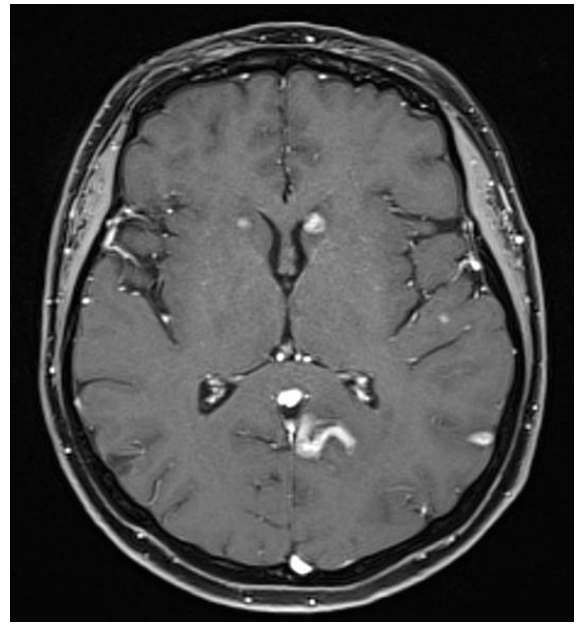
Whole Brain RT for Multiple Brain Metastases

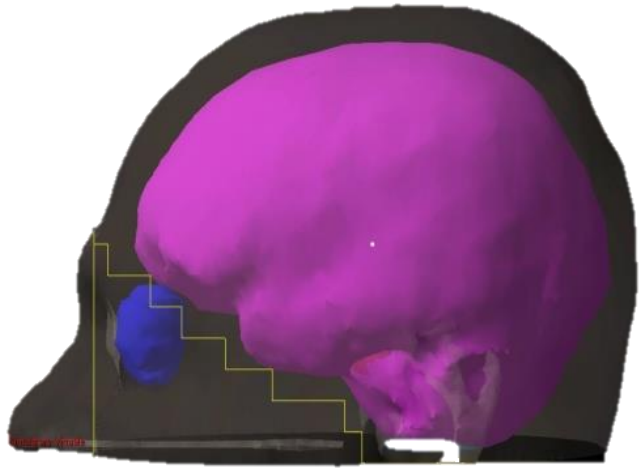
- WBI is the conventional treatment for majority of patients with (symptomatic) multiple brain metastases

- Radiation dose prescritpion
  - 30 Gy in 10 fractions
  - 20 Gy in 5 fractions
  - 37.5 Gy in 15 fractions

- Effect on survival and QoL?







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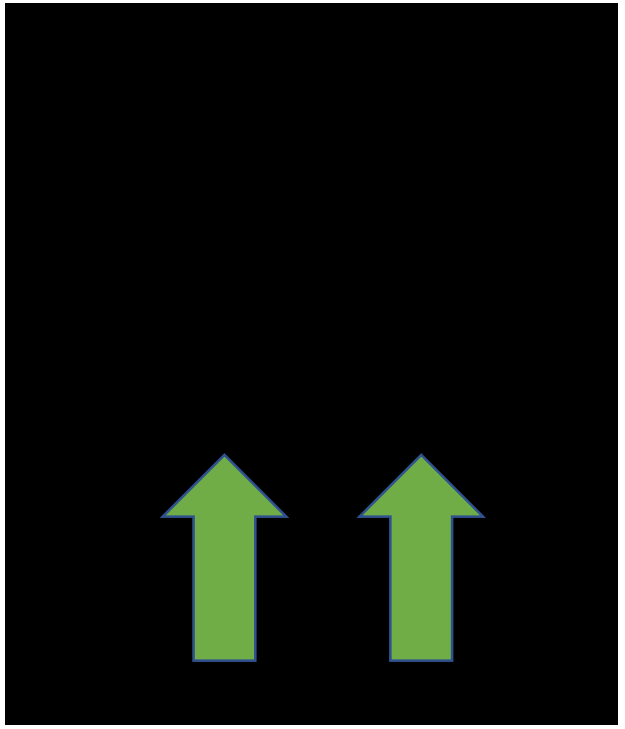
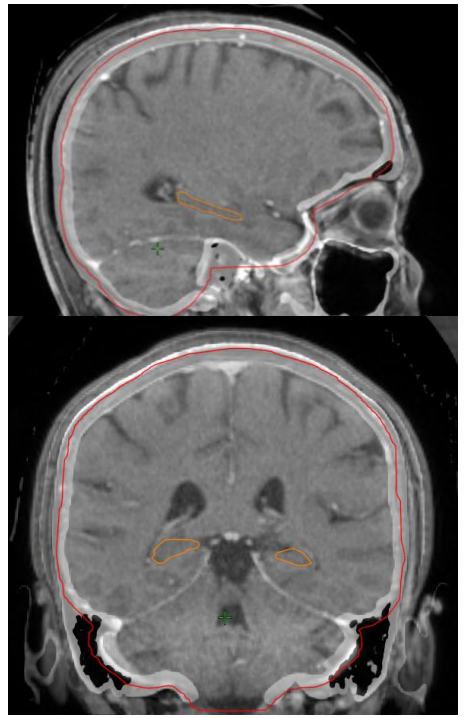
OTHER POTENTIAL APPLICATIONS
BRAIN:
ROLE OF MRI

CT imaging in the definition of hippocampal





MRI guided in the definition of hippocampal

Dosimetric impact of using a virtual couch shift for online correction of setup errors for brain patients on an integrated high-field magnetic resonance imaging linear accelerator.

Int J Radiat Oncol Biol Phys. 2017;98(3):699–708.

Ruschin M, Sahgal A, Tseng CL, Sonier M, Keller B, Lee Y.

PMID: 28581412 DOI: 10.1016/j.ijrobp.2017.03.004

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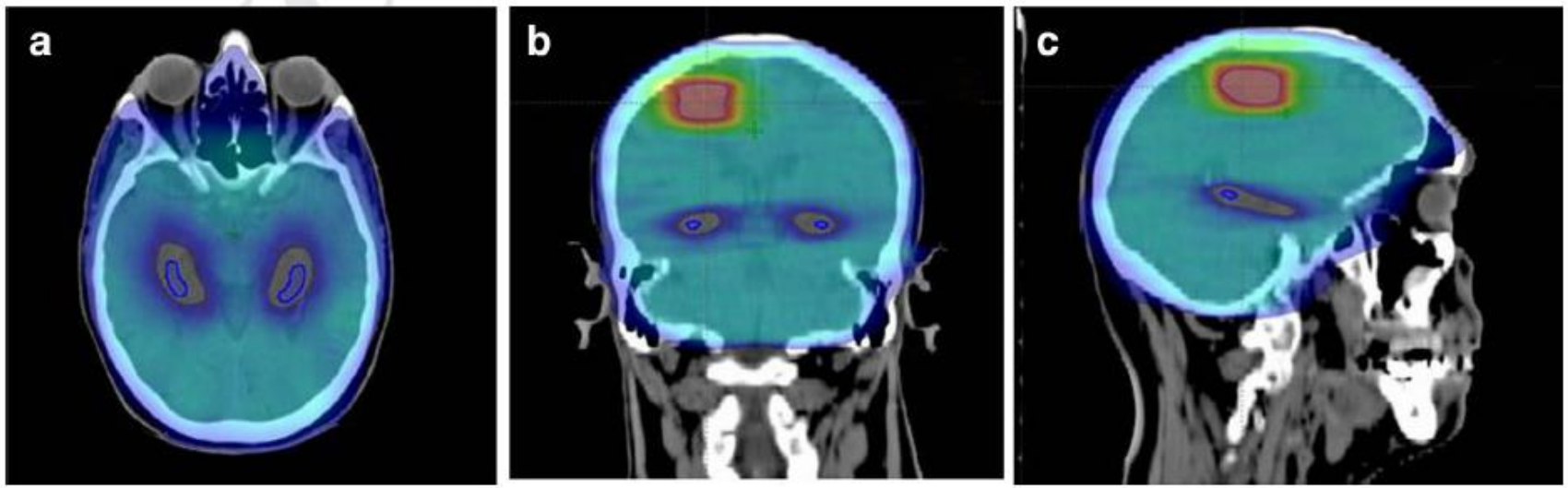
Radiol med
DOI 10.1007/s11547-015-0563-8

MAGNETIC RESONANCE IMAGING

Whole brain radiotherapy with hippocampal avoidance and simultaneous integrated boost for brain metastases: a dosimetric volumetric-modulated arc therapy study

Niccolò Giaj Levra[1] · Gianluisa Sicignano[1] · Alba Fiorentino[1] · Sergio Fersino[1] · Francesco Ricchetti[1] · Rosario Mazzola[1] · Stefania Naccarato[1] · Ruggero Ruggieri[1] · Filippo Alongi[1]



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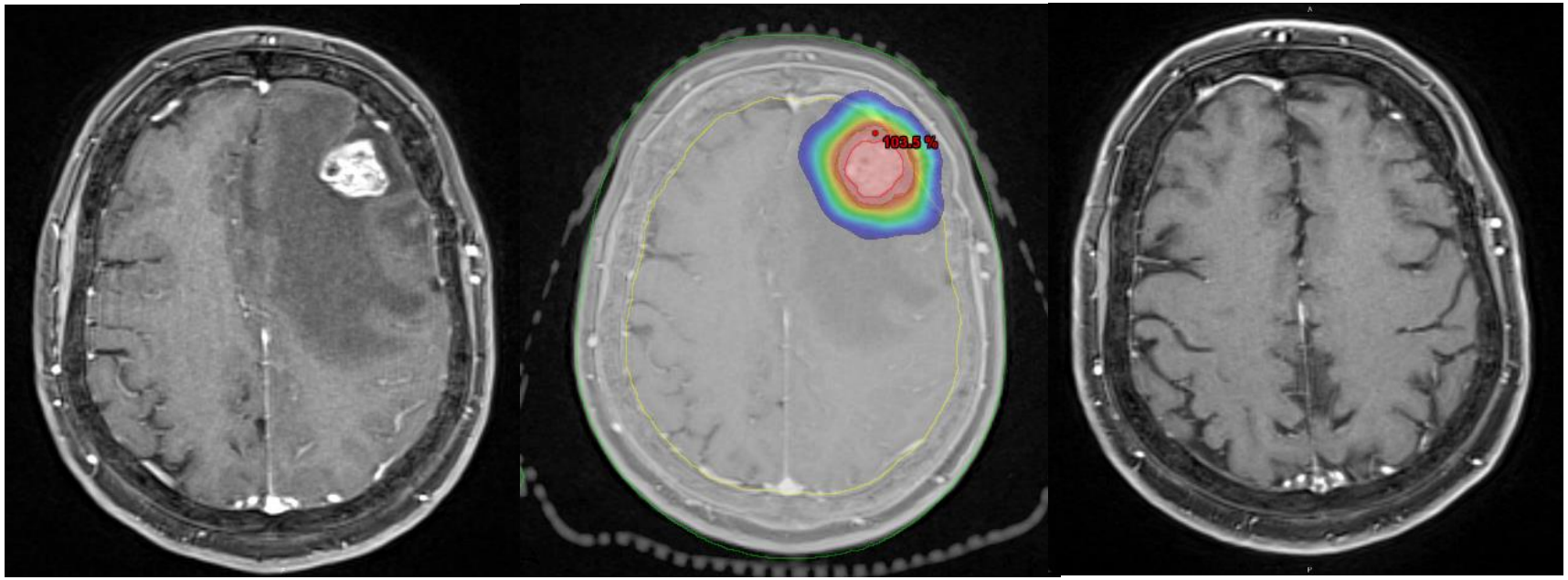
BRAIN METASTASIS IN BREAST CANCER PATIENTS: SRS

Precise delivery of high dose of radiation (> 20 Gy) to a target with a rapid dose drop off to the surrounding normal tissue

Radiosurgery is intended to provide:
- > local tumor control,
- improve clinical symptomatology,
- enhance survival.

All of these radiosurgical goals are generally achieved with:
- low morbidity,
- low cost,
- essentially zero mortality

Noyes et al, Radiosurgery 1996;
Rutigliano et al, Neurosurgery 1995



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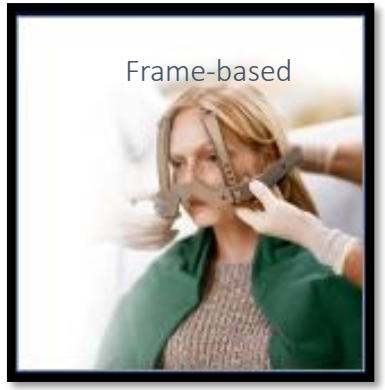
RADIOSURGERY FOR SINGLE/FEW BRAIN METS

Gamma-Knife

Invasive

Frame-based



LINAC

No frame-based

Non-Invasive

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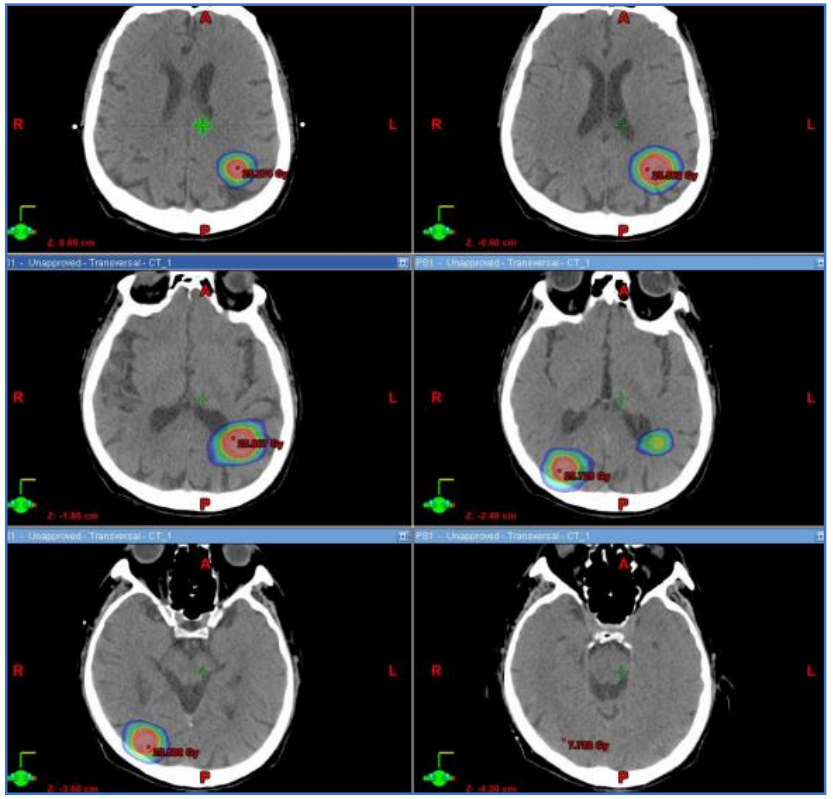
BRAIN METASTASIS: A CHALLENGING ISSUE IN CANCER TREATMENT STRATEGY

- ✓ Given systemic therapy advancements, patients live longer and approximately **20-40% of new cancer patients will develop brain metastases**.
- ✓ In brain solitary metastasis, or oligometastatic setting, **SRS has been considered a primary option** as well as surgery.
- ✓ **For multiple metastases**(>3-4), **WBRT has been considered the standard of care** and it can only increase survival between 3 and 6 months.



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Kirkpatrick et al, Neuro-oncology 2017

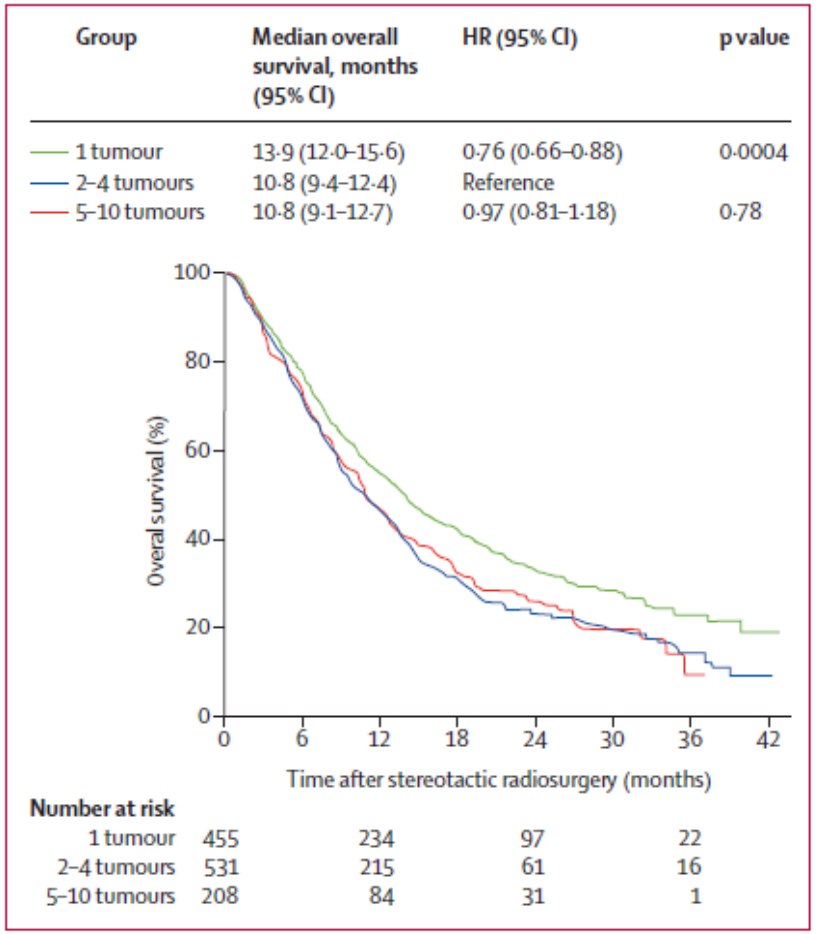
NEW «*CLINICAL*» OPTIONS FOR INTRACRANIAL RADIOSURGERY?

WBRT is really the optimal choice for >3-4 mts??

Stereotactic radiosurgery for patients with multiple brain metastases (JLGK0901): a multi-institutional prospective observational study

Lancet Oncol 2014; 15: 387–95

- ***M&M:*** *1194 pts treated with SRS (1→10 brain mets)*
- ***RESULTS:*** *Overall survival → 2-4 BM= 5-10 BM*



Group	Median overall survival, months (95% CI)	HR (95% CI)	p value
1 tumour	13·9 (12·0–15·6)	0·76 (0·66–0·88)	0·0004
2–4 tumours	10·8 (9·4–12·4)	Reference	
5–10 tumours	10·8 (9·1–12·7)	0·97 (0·81–1·18)	0·78

Number at risk				
1 tumour	455	234	97	22
2–4 tumours	531	215	61	16
5–10 tumours	208	84	31	1

Figure: **Kaplan-Meier curves of overall survival**
HR=hazard ratio.

Interpretation Our results suggest that stereotactic radiosurgery without WBRT in patients with five to ten brain metastases is non-inferior to that in patients with two to four brain metastases. Considering the minimal invasiveness of stereotactic radiosurgery and the fewer side-effects than with WBRT, stereotactic radiosurgery might be a suitable alternative for patients with up to ten brain metastases.

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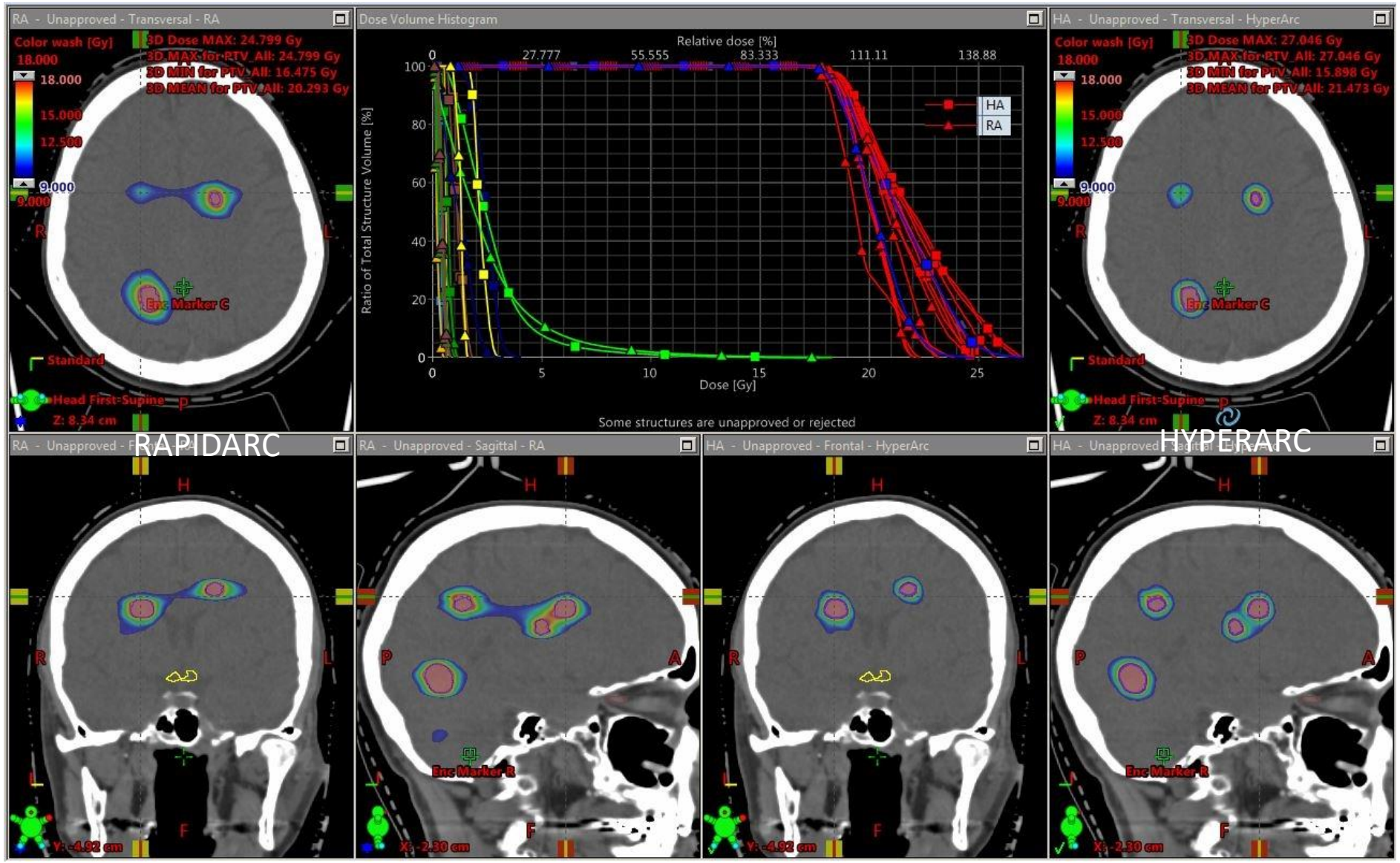
Yamamoto et al. Lancet 2014

HYPERARC MULTIMETS PLAN COMPARISON: CLINICAL CONSIDERATIONS

In case of multiple metastases, when compared with Rapidarc plan (one isocenter per lesion) non coplanar HyperArc (1 isocenter for all lesions)solution was able to:

- ✓ reduce drammatically treatment time(beam on time & time in/out patient),
- ✓ significantly reduced $V_{12,}$ while an equivalent mean dose to the brain out is assured,
- ✓ significantly obtain gain in reducing GI and improving CI to PTV_{all}

Multiple lesions, pt. #1



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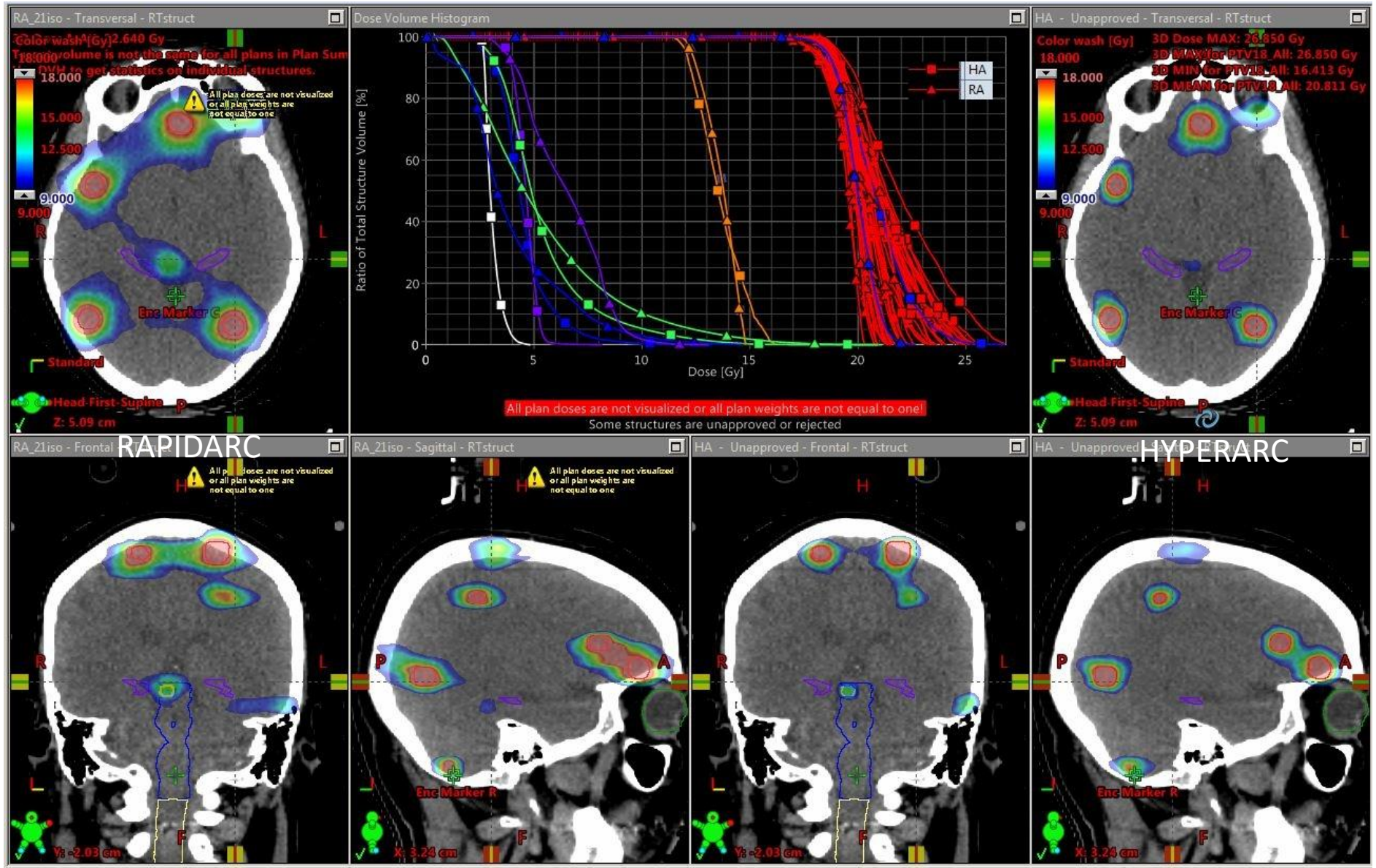
Multiple lesions, pt. #2



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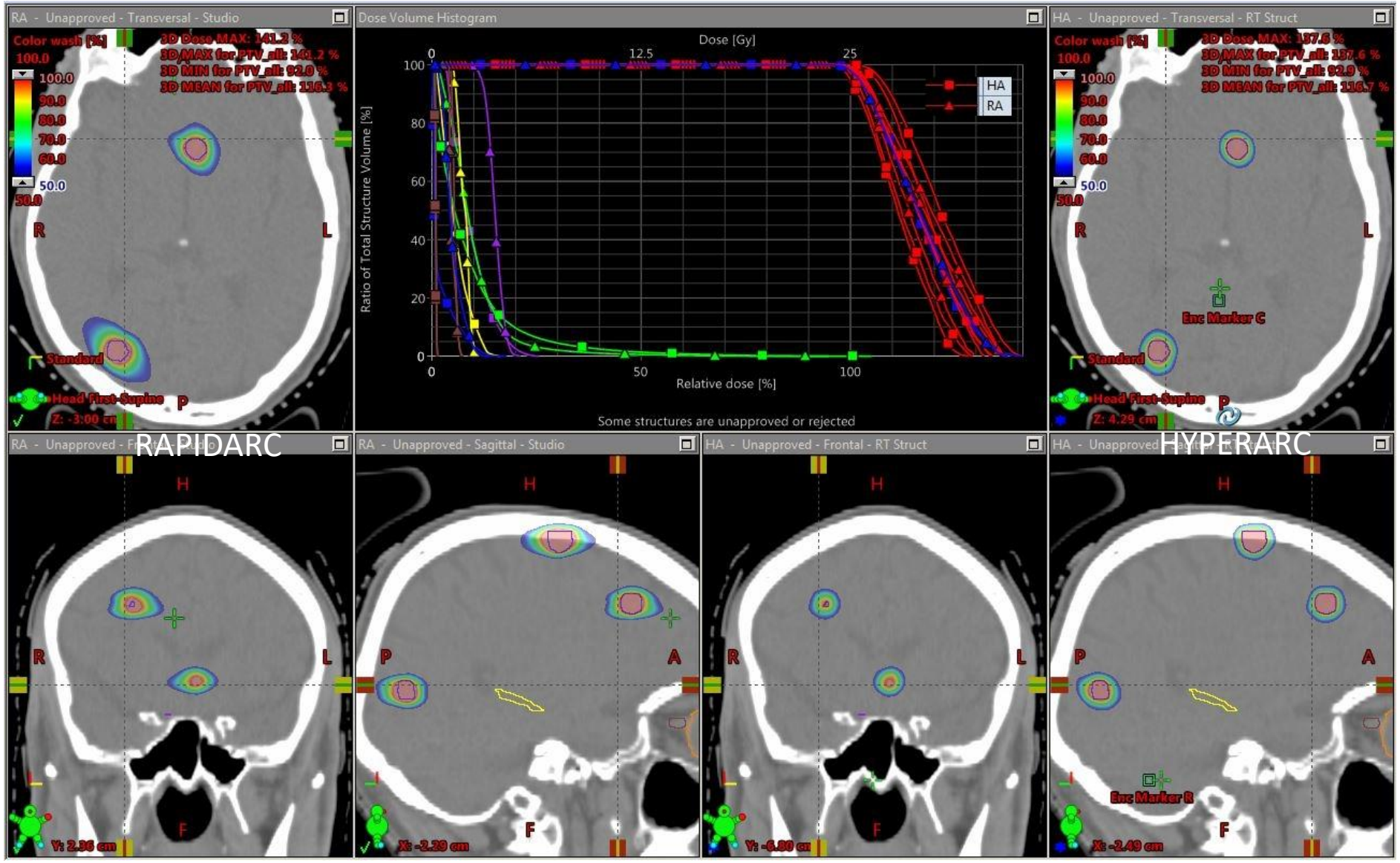
Multiple lesions, pt. #3



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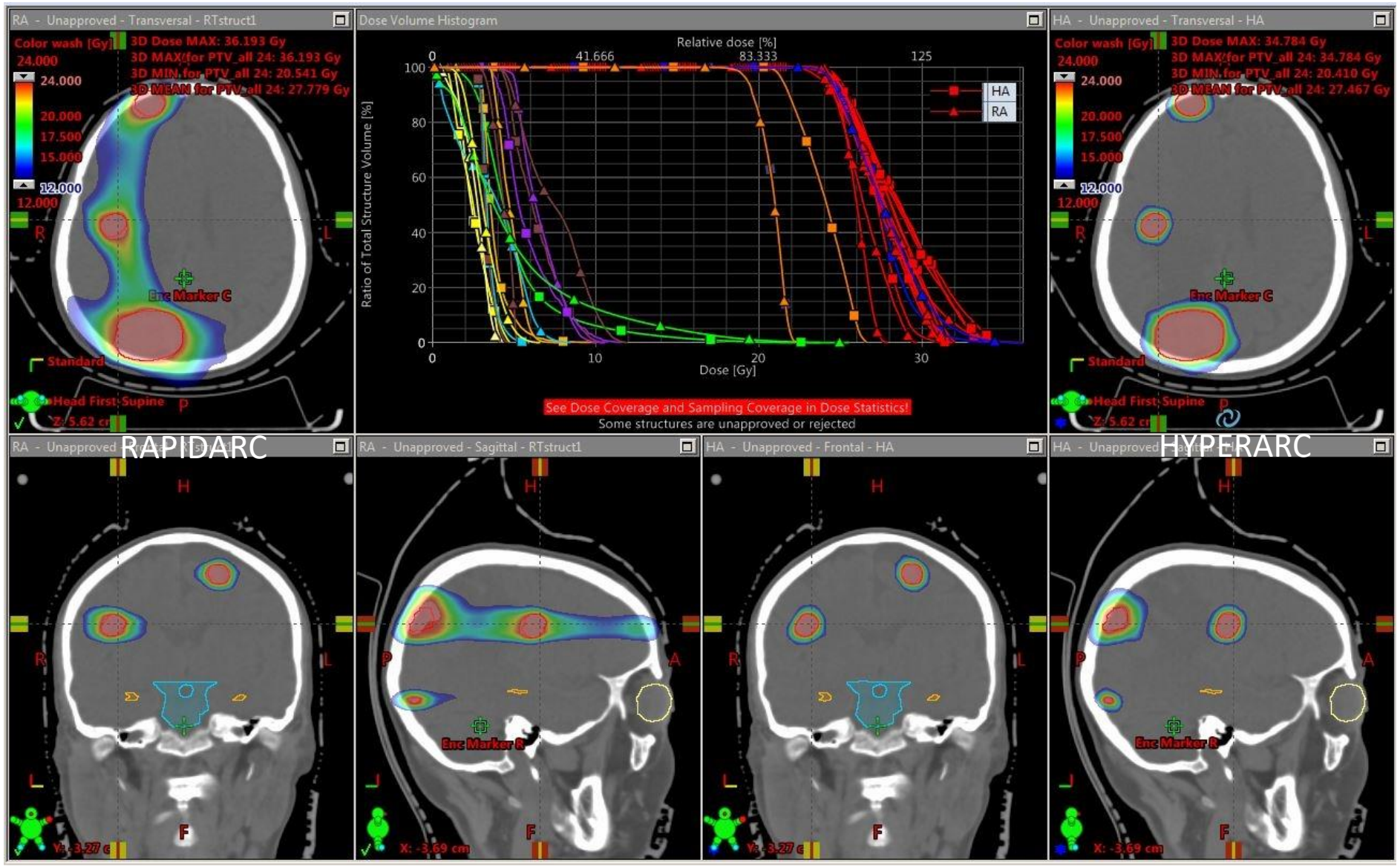
Multiple lesions, pt. #5



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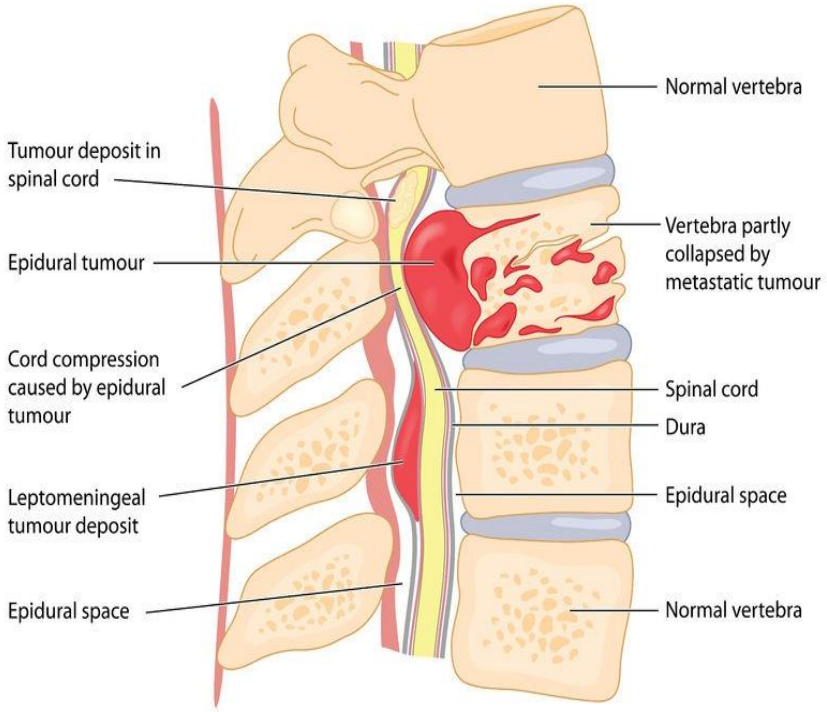
SPINE METASTASES:

INCIDENCE OF THE PHENOMENON

- Approximately **one third** of all cancer patients will develop bone metastases and approximately ***70%*** will present metastases **involving the vertebral column**.
- **Back pain** is the most common initial presenting symptom, often with associated neurological problems.
- When undertreated, spinal metastases may cause vertebral body fracture, radiculopathy, **debilititating complications** of epidural spinal cord compression.

Van Oorschot et al., 2011



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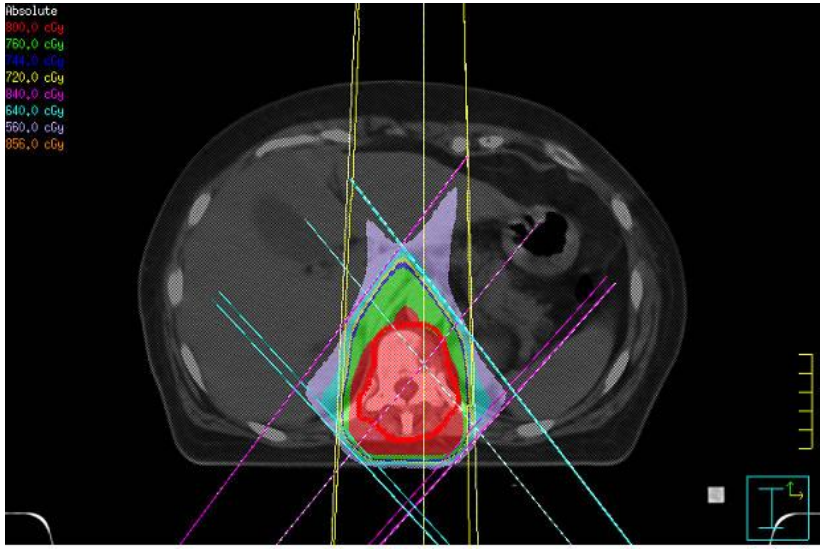
SPINE METASTASES:

ROLE OF CONVENTIONAL RADIOTHERAPY



- **RT has an historical role** in the management of spine metastases and the most commonly used regimen of RT is 30 Gy in 10 fractions .

- **Single-dose** treatments are usually preferred in patients with a limited lifespan and/or poor performance status or in case of long waiting lists of the treating centers.

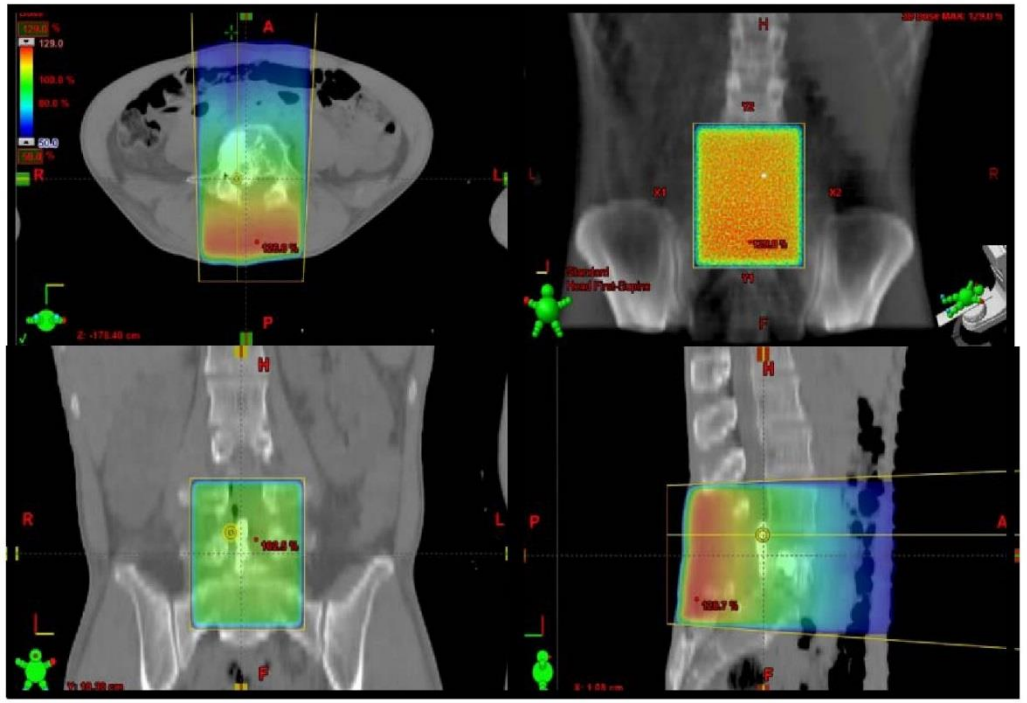
  Lutzet al., 2007

SPINE METASTASES:

LIMITS OF CONVENTIONAL RADIOTHERAPY

- **Efficacy of Conventional RT** is low:
- CR:0-20%
- PR:60%
- LC: 45%

Rades 2010; Zeng 2012 Zeng 2012; Nguyen 2011; Chow 2007; Mizumoto 2011.



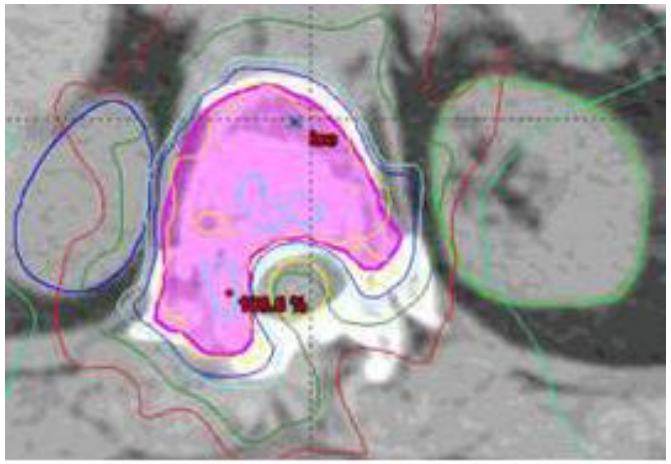
SPINE METASTASES:

EMERGING ROLE OF SRS/SBRT

Stereotactic body radiotherapy for de novo spinal metastases: systematic review J Neurosurg Spine. 2017

International Stereotactic Radiosurgery Society practice guidelines

Zain A. Husain, MD,[1] Arjun Sahgal, MD,[2] Antonio De Salles, MD,[3] Melissa Funaro, MS, MLS,[4] Janis Glover, MLS,[4] Motohiro Hayashi,[5] Masahiro Hiraoka, MD,[6] Marc Levivier, MD,[7] Lijun Ma, PhD,[8] Roberto Martínez-Alvarez, MD,[9] J. Ian Paddick, MSc,[10] Jean Régis, MD,[11] Ben J. Slotman, MD, PhD,[12] and Samuel Ryu, MD[13]



- Local control ~ 90% at 1 year
- Complete pain control > 50%
- Low toxicity profile:
  - Vertebral compression fracture 9,5%
  - Symptomatic myelopathy 0,2%

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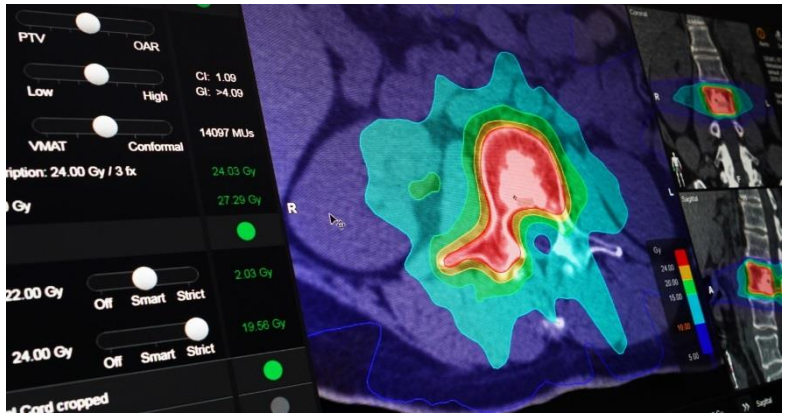
SPINE METASTASES:

NOVALIS ELEMENTS SPINE SRS @Negrar

ELEMENTS SPINE SRS is a solution able to:

- Optimal multi-images *Allignement* (PET and/or MRI and simulation CT)
- *Autosegmentation*, delineating Targets (GTV-PTV) as the sectors at risk according to the International spine radiosurgery consortium guidelines
- SBRT Planning designed to obtain incredibly *sharp dose gradients* to deliver as high dose as possible to the target volume while respecting the constraint of the critical structures, considering that the spinal cord/thecal sac is the dose limiting structure.



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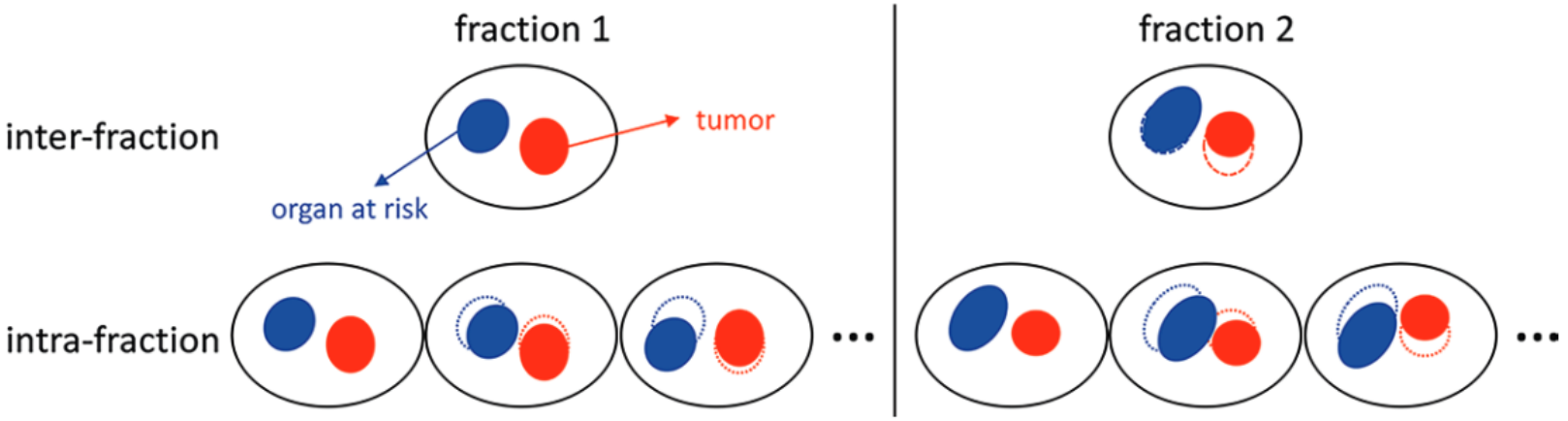
Potential uncertainties in Radiation Oncology could affect results and tolerability



Ricardo Otazo et al. Radiology 2021

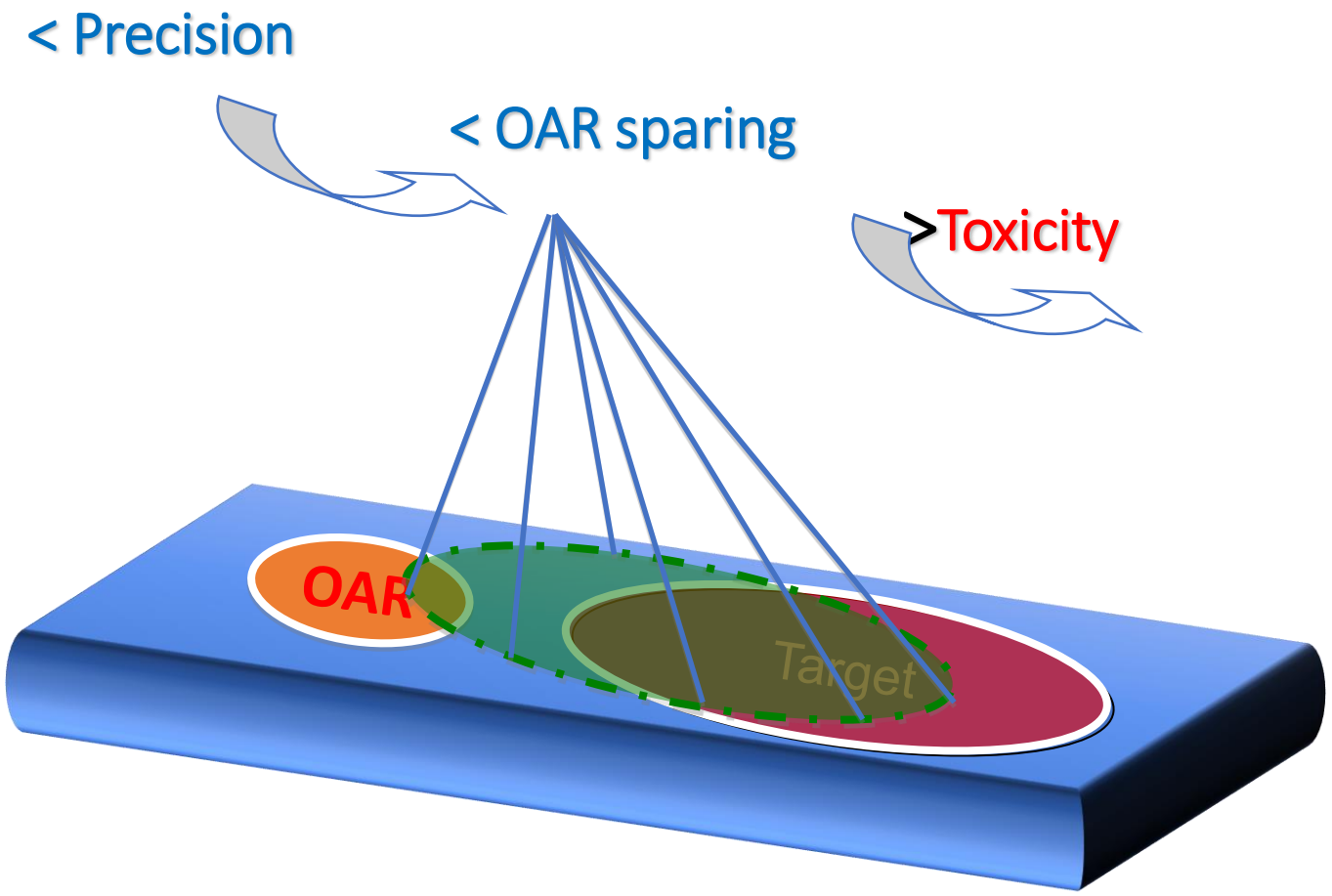
Potential uncertainties in Radiation Oncology could affect results and tolerability

> Precision

> OAR sparing

Dose escalation

Potential uncertainties in Radiation Oncology could affect results and tolerability



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IGRT

NATURE REVIEWS | CANCER

Innovations in image-guided radiotherapy

Dirk Verellen, Mark De Ridder, Nadine Linthout, Koen Tournel, Guy Soete and Guy Storme

At a glance

- In order to assure proper coverage of the clinical target volume (CTV) by radiation, a margin needs to be added to compensate for daily positioning errors and internal motion of organs, resulting in the planning target volume (PTV). The PTV therefore includes normal tissues near the tumour, to which radiation is intentionally delivered.
- The dose of radiotherapy that is necessary to control a tumour is often not delivered because of a high probability of complications in nearby normal tissues. This problem can be tackled by the generation of conformal dose distributions that tightly match the volume of the PTV and/or by decreasing the amount of normal tissue in the PTV.
- Image-guided radiotherapy (IGRT) is defined as frequent imaging in the treatment room that allows treatment decisions to be made on the basis of these images. IGRT aims at decreasing CTV-to-PTV margins from centimetres to millimetres.
- The synergy between conformal radiotherapy (CRT) and IGRT has drastically improved the quality of radiotherapy and has broadened its possibilities and indications. Clinical implementations of CRT–IGRT have enabled dose escalation, conformal sparing and non-uniform dose distributions, and initiated a revision of fractionation schedules.
- Research to improve image quality in radiotherapy is not new, but developments of software to quantify target localization errors, on the basis of in-room imaging and hardware allowing automated set-up, have stimulated mainstream clinical application of IGRT.
- IGRT makes use of many different imaging techniques, using modalities ranging from planar imaging to fluoroscopy to cone-beam CT, and following procedures as simple as using a single set-up image or as complex as intra-fraction tumour tracking.
- IGRT can be applied for managing of inter-fraction as well as intra-fraction geometric set-up uncertainties and for adapting treatments to tumour responses.

A CONTINUOUS CHANGING:
IMAGING ON BOARD (IGRT)

Imaging 2-D: → **Imaging 3-D:**

MV imaging

KV imaging

Cone Beam CT imaging

ADVANCED TECHNOLOGIES IN IMAGE-GUIDED RADIATION THERAPY

Balter J et al., Seminars in Radiation Oncology, 2007

IGRT advantages

- PTV margins substantially decreased
- Substantial reduction in irradiated volume
- Better sparing of organ at risk

Decreases Toxicity

- Higher doses to the tumor
- Increases the possibility to use non conventional fractionation (SBRT)

Improves local control rates

Precision Radiation Oncology: The Era of Hybrid Linac…

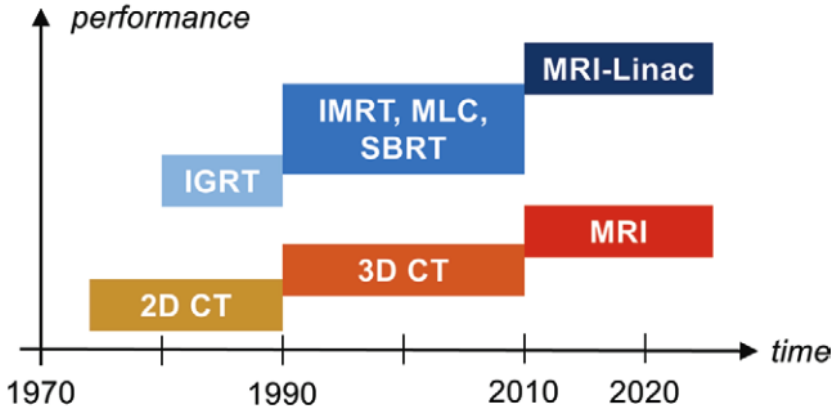

Figure 1: Evolution of image-guided radiation therapy (RT) methods (in blue shades) and corresponding imaging technique used for guidance (yellow, orange, red). IGRT = image-guided RT, IMRT = intensity-modulated RT, MLC = multileaf collimator, MRI-Linac = MRI-guided linear accelerator, SBRT = stereotactic body RT, 3D = three-dimensional, 2D = two-dimensional.

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ADVANCED RADIATION ONCOLOGY DEPARTMENT IN NEGRAR-VERONA, ITALY

RADIATION ONCOLOGY 2

1.5 T MR-LINAC ELEKTA UNITY

1.5T MRI SIMULATOR DEDICATED TO RT PHILIPS

Elekta Unity Reference Site

Elekta

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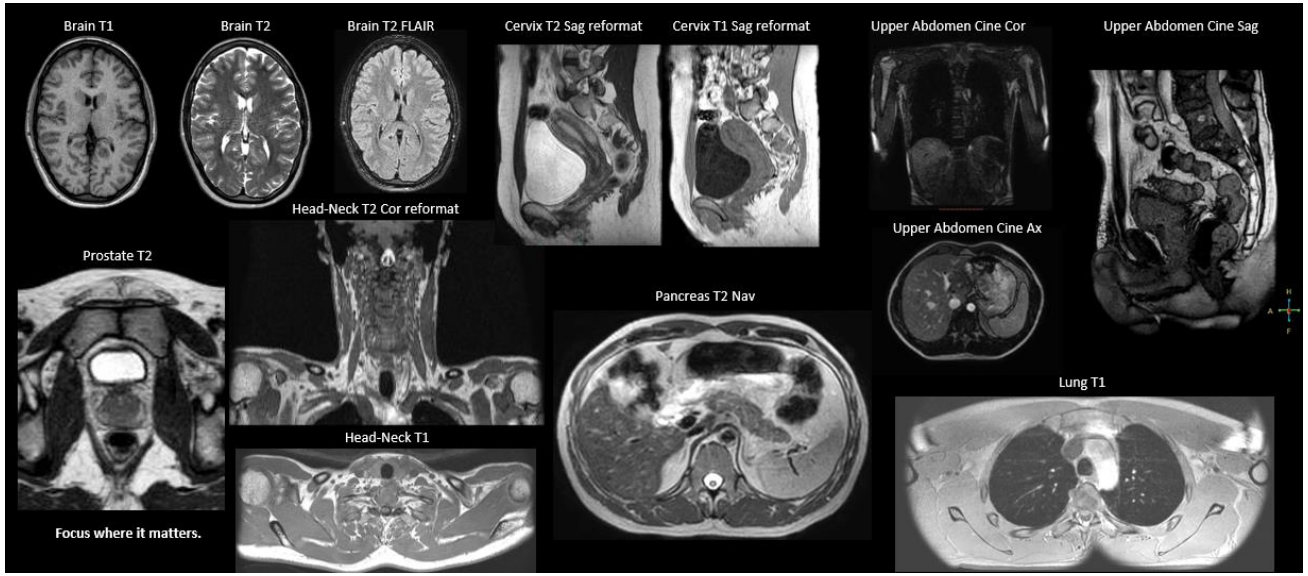
Advanced Radiation Treatment with MRI-Guided Linear Accelerator (MRI-LINAC)



MRI-based imaging on a linear accelerator offers superior high-definition image quality, especially for some soft tissue cancers, as compared to traditional linear accelerators

MRI-LINAC can adapt the radiation treatment plan based on movement of the tumor or your organs, and also track the motion of the tumor

Increased accuracy and precision with the ultimate goals of reducing the amount of radiation exposure to surrounding organs and reducing potential side effects

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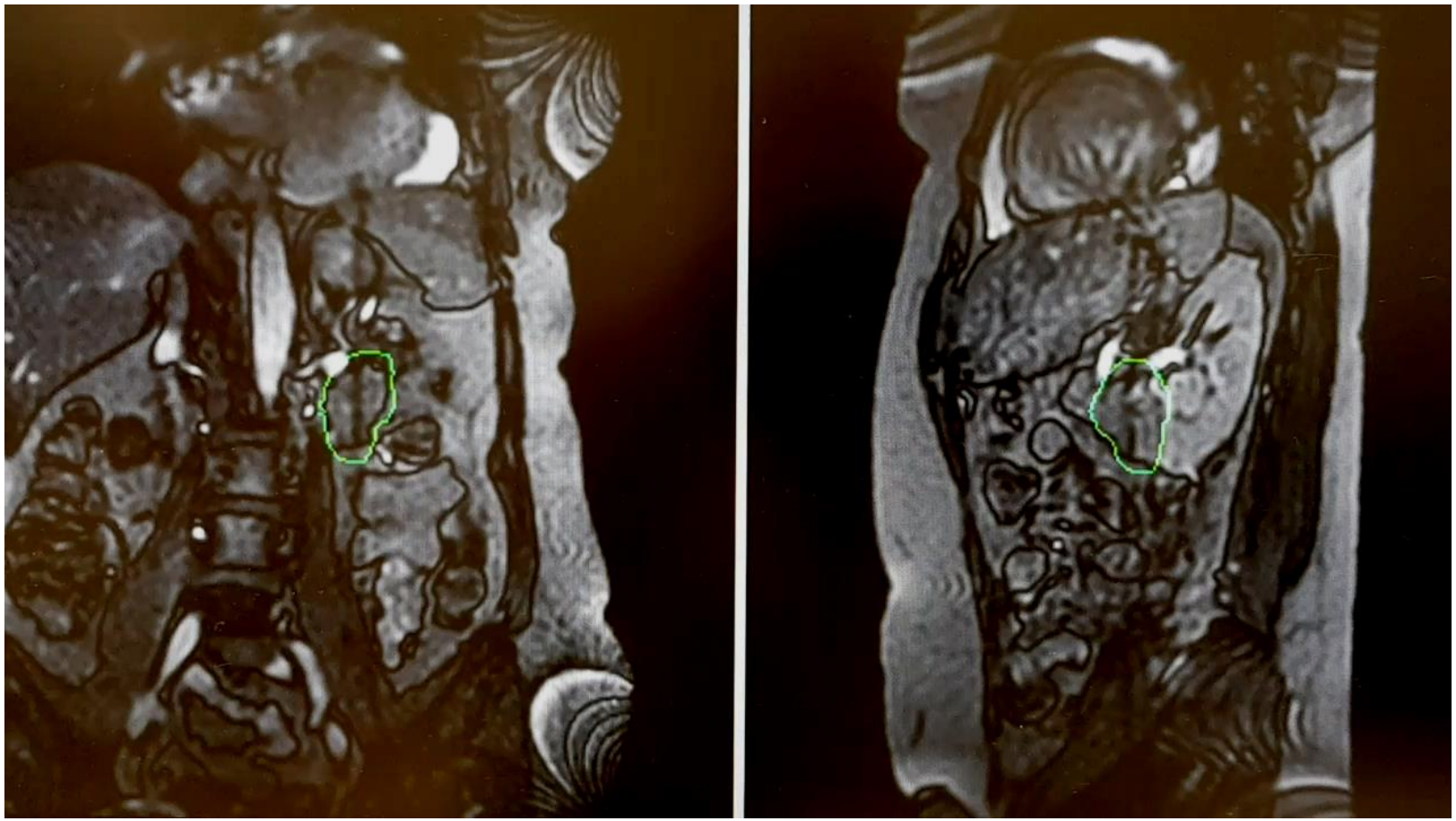
b3DVaneXD and Motion Management in SBRT on left kidney secondary malignancy from Breast cancer



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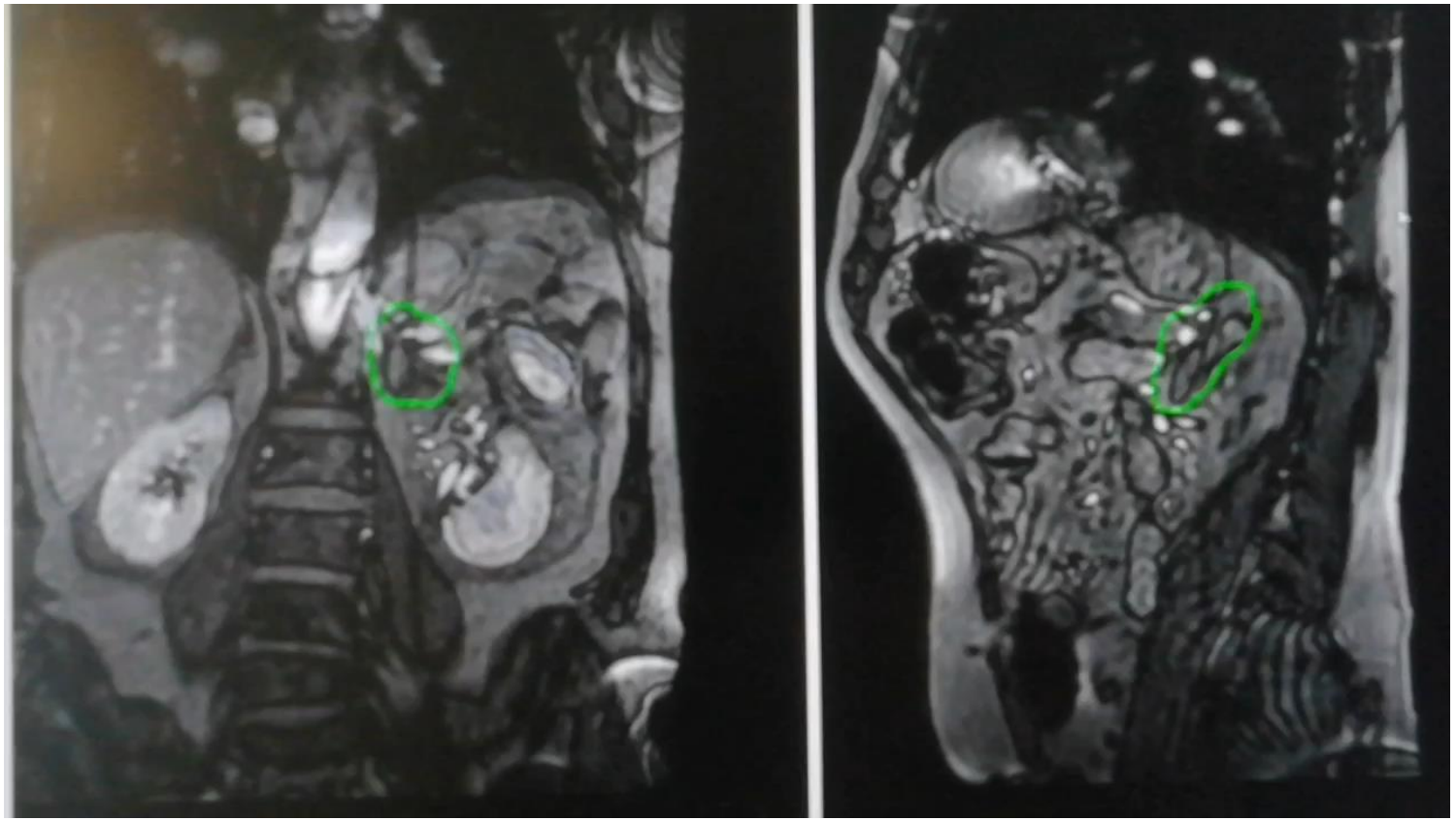
MOTION MANAGEMENT IN ADRENAL GLAND SBRT

Treatment delivery and motion management



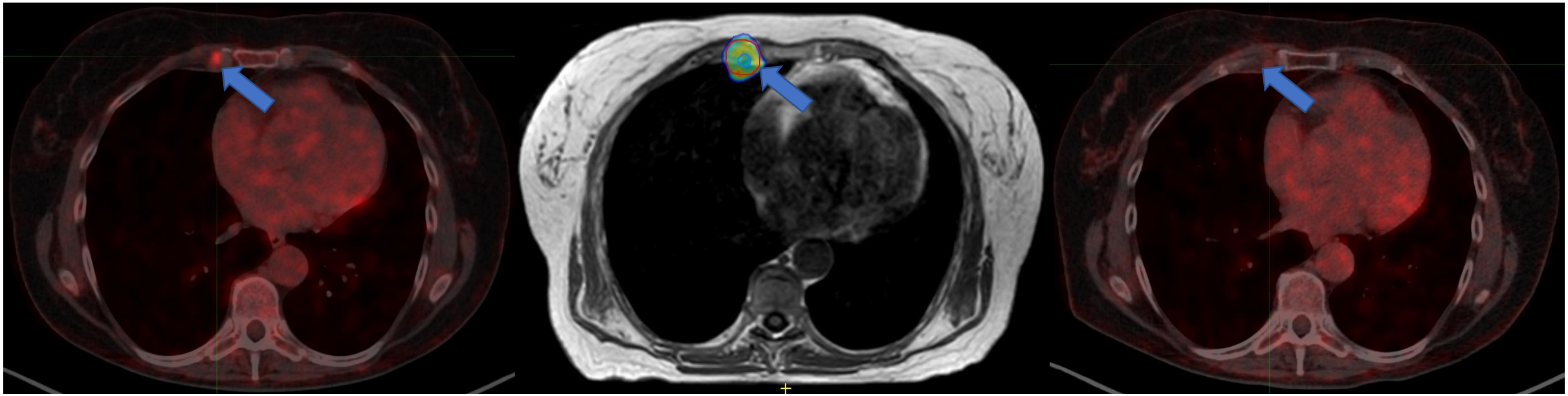
T1DVaneXD over Motion Management: use of the edge enhancement of the chemical shift due to the balanced scans (Planning and Verification) helps, by improving the correlation between imaging types, to monitor the extension of movement of the PTV

INTERNAL MAMMARY LYMPH NODE METASTASES from breast cancer

PET-CT PRE-SBRT

RM-SIM SBRT (40 Gy / 5 fr)

PET-CT POST-SBRT



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How technology could optimize clinical outcomes in Radiation Oncology?
Main aims…

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