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IPOFRAZIONAMENTO E TECNICHE INNOVATIVE

*29 Aprile 2014*

# 4D-CT, PET, RM NELLA DEFINIZIONE DEL PIANO DI TRATTAMENTO

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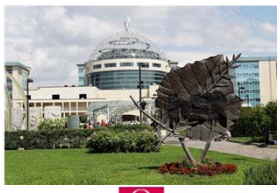


OSR

OSPEDALE SAN RAFFAELE
ISTITUTO DI RICOVERO E CURA A CARATTERE SCIENTIFICO

## Argomenti

- Ruolo ed evoluzione dell'imaging in RT oncologica
- Immagini per il planning in RT: caratteristiche
  - CT, NMR, PET
- Il problema del movimento (respiratorio)
  - Qualità imaging
  - Definizione margini
  - Accuratezza dosimetrica
- Esempio di "contenuto radiobiologco" imaging:
  - ca esofago, "tessitura" distribuzione tracciante come indice di radiosensibilità
- Esperienza OSR utilizzo imaging multimodale nella definizione/ottimizzazione/'adaptive' piano RT

## Ruolo dell'imaging in radioterapia oncologica

→ dall'anatomia alla "valenza" radiobiologica

- Corretta stadiazione e scelta strategia terapeutica ottimale

✓Accurata delineazione dei volumi [ICRU 50-62]

- GTV="gross tumor volume"
- OAR="Organ at Risk"

.... zone a diversa radiosensibilità

✓ Valutazione dei margini [ICRU 50-62, BIR 2003]

- PTV="Planning Target Volume"
- RV="Planning risk volume"

.... incertezze geometriche

- Verifica corretta esecuzione del trattamento
- Individuazione parametri predittivi della risposta a RT
- Valutazione 'precoce' effetto trattamento radiante

→ ADAPTIVE RADIOTHERAPY

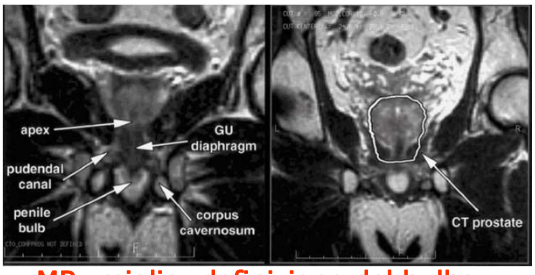
## GTV: diagnostica "ottimale"

| SEDE | MODALITA' |
|---|---|
| Polmone<br>LN mediastinici<br>Apice | CT+IV<br>PET<br>NMR |
| Prostata | US transrettale<br>NMR |
| Vescica | CT |
| CNS<br>Residuo/recidiva | NMR<br>PET |
| Mammella<br>Recidiva | Mammografia<br>US<br>NMR |

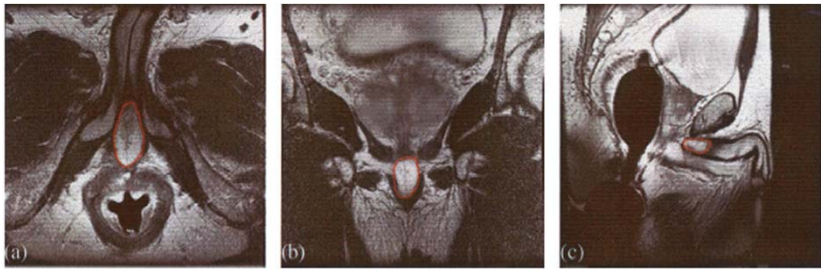
Carey, Estro Teaching Course 2002

LN= Linfonodi
CNS= Sistema Nervoso Centrale
IV= Mezzo di contrasto
PET=Tomografo ad emissione di positroni
US=Ultrasuoni
NMR=Risonanza Magnetica Nucleare

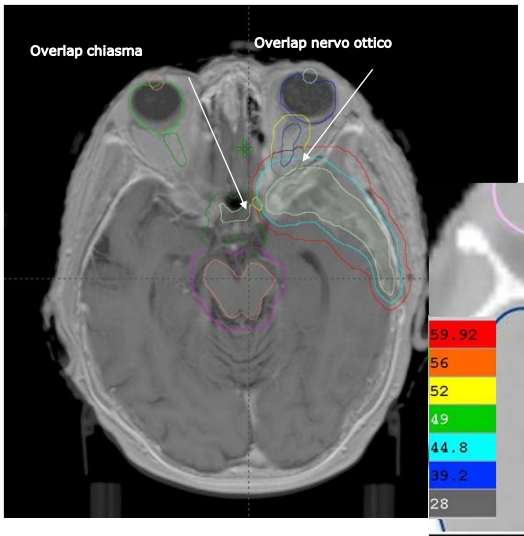
## MR: miglior definizione dell'apice prostatico




## MR: miglior definizione del bulbo

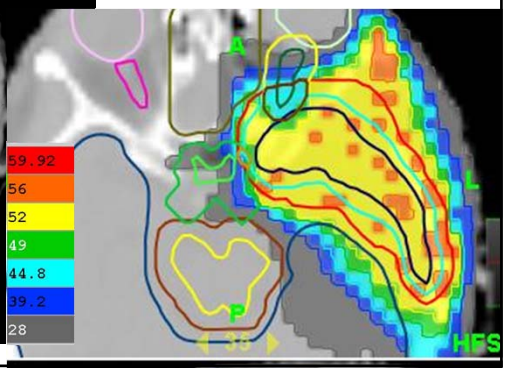



## Esempi applicativi di pianificazione RT su immagini di fusione TC-RM: distretto encefalico




### Planning HT

Dprescrizione PTV: 54 Gy
Constraint nervo ottico: 50 Gy
Constraint chiasma: 50 Gy



## Verso BTV ("biological target volume")

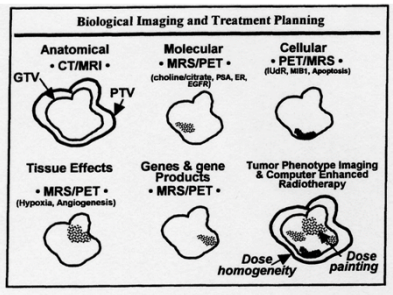
Barret A
Estro teaching course, 2002

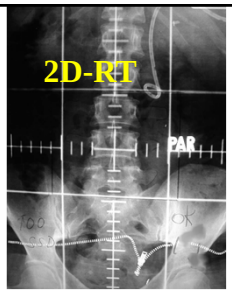
Potenzialità imaging multimodale

- stato funzionale, metabolico, molecolare
- MR funzionale , spettroscopica , etc
- PET con traccianti sensibili biologia tumorale :

Componente ipossica

- Angiogenesi tumorale
- Ripopolazione durante il trattamento
- etc

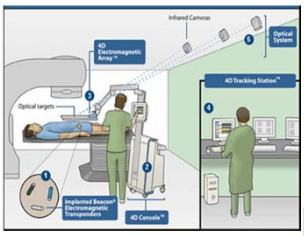



## SVILUPPO TECNOLOGICO IN RT

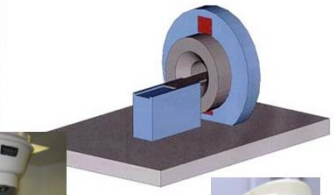
| Cronologia | Tecnica RT | Definizione Volumi di Trattamento | Verifica set-up |
|---|---|---|---|
| <1990 | 2D-RT | Rx | Rx |
| Anni '90 | 3D-RT | CT | Rx , EPID |
| >2000 | IMRT e IGRT | CT , PET , MR | EPID , kV-CT , MV-CT Sistemi ottici, US, etc |

## Tecnologia RT (fotoni): delivery and IGRT …







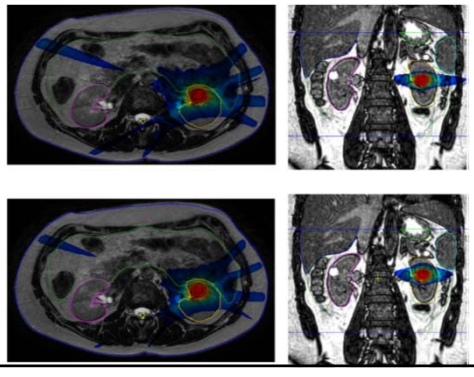


ESTRO 33, 2014

SP-0204
**Online MRI guided 4D-SBRT of thoracic and abdominal tumours**
G.J. Meijer[1], C.A.T. Berg[1], B.W. Raaymakers[1], M. Van Vulpen[1], J.J. Lagendijk[1]
[1]*UMC Utrecht, Department of Radiotherapy, Utrecht, The Netherlands*

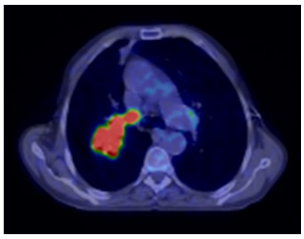
imaging within or just prior to dose delivery. In our institution the building of the 2nd prototype of our MR-linac was recently completed. This system combines a 6MV linear accelerator mounted on a gantry with a 1.5T MR scanner and allows onsite MR image acquisition with simultaneous dose delivery. MRI has been proven to be an extremely versatile imaging technique in three ways.

**Dosimetric feasibility of MRI-guided external beam radiotherapy of the kidney**

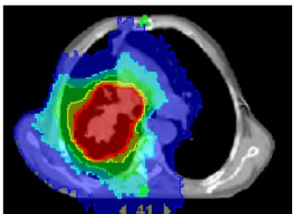


Stam el al PMB 2013

## IMRT (Intensity Modulated Radiation Therapy )
## IGRT ( Image Guided Radiation Therapy )



PET/TC



IMRT

MV-CT

- accurata definizione del target (PET/CT ; NMR/CT; etc )
- migliore conformazione della dose ( IMRT )
- migliore controllo del set-up ( KV-CT, MV-CT, sistemi fluoroscopici, sistemi ottici, US, etc )
- possibilità di dose per frazione più elevata (ipofrazionemento, "concomitant boost", etc.)
- ridotta tossicità

## Immagini per planning RT:

- **CT: Immagine di riferimento per planning RT**
  - **Densità elettroniche (calcolo dose) & Ridotta distorsione spaziale**
    - **ma …**
  - **possibili effetti distorsivi dovuti a protesi, mdc, aria,**
  - **rappresentazione anat. di un "momento"**
  - **effetti respirazione, deformazione organo,**

- **Modalità di acquisizione CT ("di centratura") :**
  - **Posizionamento paziente come in terapia; lettino "piatto"; sistema di immobilizzazione; tatuaggi cutanei ;lasers di posizionamento**
  - **Eventuali istruzioni/protocolli per modalità respirazione e riempimento organi**
  - **Assenza (riduzione) mezzo di contrasto**
  - **Risoluzione nel piano < 1 mm**
  - **Distanza slices (determina qualità DRR):**
    - **dipende dal distretto anatomico 1-3 mm**
    - **può aumentare fuori dal target**
  - **Includere l'intera estensione degli organi a rischio (per corretta valutazione istogramma dose volume)**

## Immagini per planning RT:

- **MRI**
  - **"Mappatura" spaziale distribuzione protoni**
  - **Imaging multiplanare e volumetrico**
  - **Sequenze ultraveloci**
  - **Potenzialità infomazioni funzionali e fisiologiche**
  - **Imaging d'elezione per tessuti molli**
  - **Contrasto limitato in presenza di strutture ossee o calcificazione**
  - **Complementare a CT per diversi distretti**
  - **Può essere l'unica modalità diagnostica nei trattamenti intra cranici**
  - **Posizionamento come in terapia**
  - **Valutazione /risoluzione distorsioni**
  - **Assenza densità elettroniche:**
    - **coregistrazione con CT**
    - **assegnazione densità a parti/ tessuti/ organi**
  - **Crescente interesse verso utilizzo informazioni "spettroscopiche"**

## RM: molteplici procedure

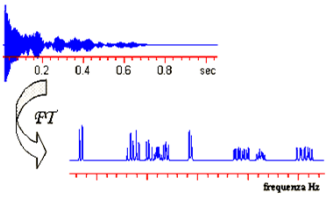
•Studio morfologico (**MRI; T1 e T2 pesate, mdc**)

•Studio pesato in diffusione (**DW-MRI,;ADC**)

•Studio pesato in perfusione (**PW-MRI,; angiogenesi. etc**)

•Studio spettroscopico dell'idrogeno (**MRSI, individuazione metaboliti**)

•Functional MRI (**fMRI;** cquisizione veloce di molte immagini dinamiche

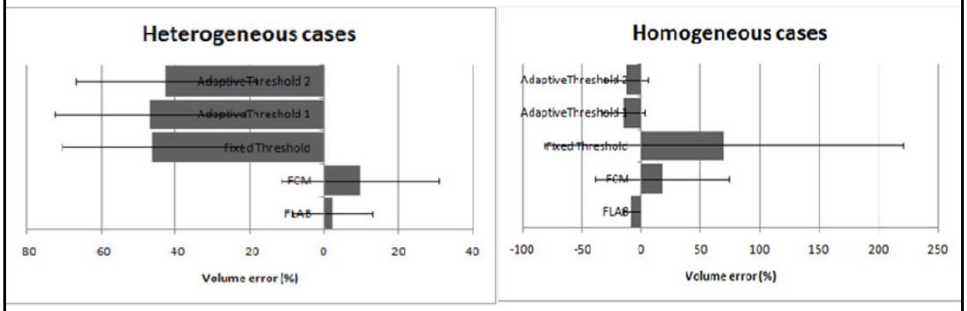


# Immagini per planning RT:

## PET ("Positron Emission Tomography")

- **Tecnica diagnostica funzionale**
- **Rappresentazione tomografica distribuzione radioattività (emettitori di positroni)**
- **Rilevazione in coincidenza spaziale e temporale di due fotoni (511 KeV) emessi a seguito di reazione di annichilazione.**
- **Acquisizione dati trasmissivi per determinazione mappa di attenuazione**
- **Ridotta risoluzione spaziale (3-5 mm) anche nel piano transassiale**
- **Da validare la procedure per la definizione "quantitativa" dei volumi**
- **Sistemi integrati TAC-PET**
  - **più accurata stadiazione**
  - **migliore definizione del T e N**
  - **migliore definizione del movimento d' organo ( 4D-PET/TC )**

Metodi per la delineazione dei volumi (GTV) su immagini PET
…. tentativi di superare la delineazione fatta da MN esperto




Metodi:
-Soglia fissa
- Soglia adattiva (2)
-Metodi statistici "avanzati" (FCM, FLAB)

Le Maitre et al. PMB 2012

## Anatomia: la 4-D dimensione. Scala dei tempi delle variazioni anatomiche

**FOCUS ON**
**Anatomical changes induced by respiratory motion (thorax, abdomen)**

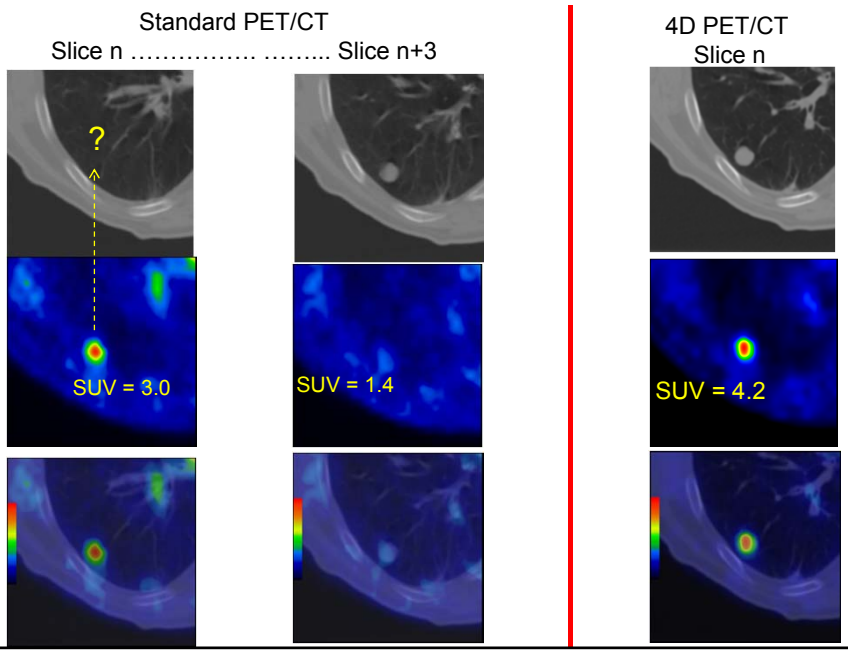
Organ motions

Table 1 Anatomic "Motions" and the Timescale at Which They Occur

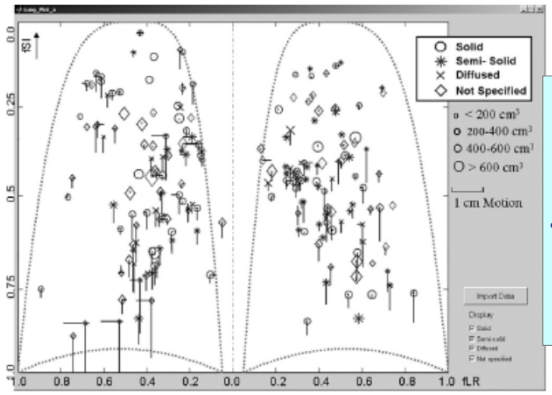
| | | |
|---|---|---|
| Day to day | Skin motion | Nonpredictable |
| Hour to hour | Prostate motion | Nonpredictable |
| Minute to minute | Bladder filling | Predictable |
| | Neck flex | Nonpredictable |
| Second to second | Respiration | Predictable |
| | Heartbeat | Predictable |
| | Peristalsis | Nonpredictable |

M van Herk SRO 2007

## Movimento e qualità immaginiPET/CT Vs 4D PET/CT

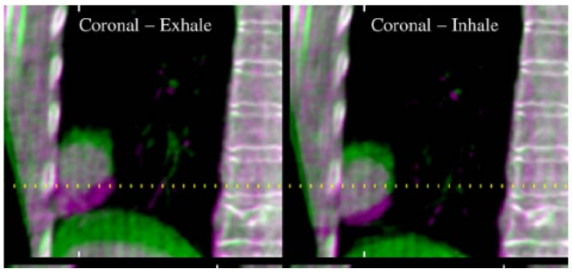


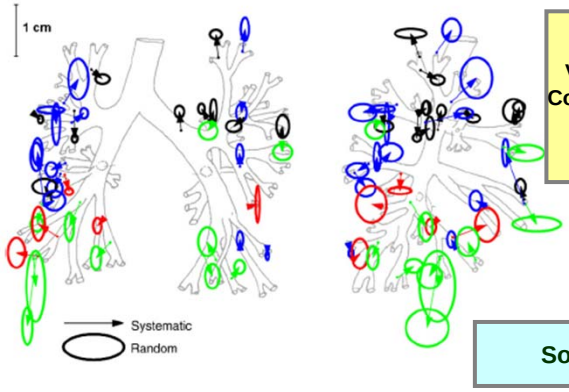
# Tumore polmonare: mov intrafrazione




- 166 cases
- Tumor Movement > 5 mm
  SI: 40 % (PTs)
  AP / LR: < 6 % (PTs)
- Tumor Movement > 10 mm
  < 10 % (PTs)

[Liu IJROBP 2007]

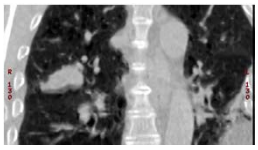


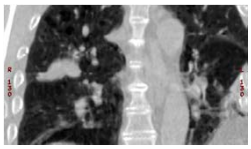

Varazione posizione tra frazioni
Componente sistematica e random

Sonke IJROBP 2008

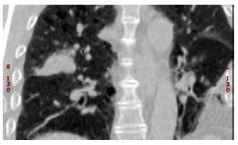
## 4D CT
## Individuazione data-set di riferimento per PLANNING RT



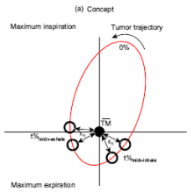
Phase 1



Phase 2

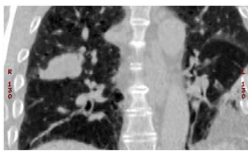


Phase 3

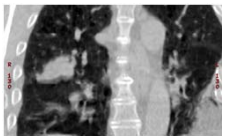



Mid-VENTILATION: A dataset close to the time-weight mean-position

Phase 5



Phase 6



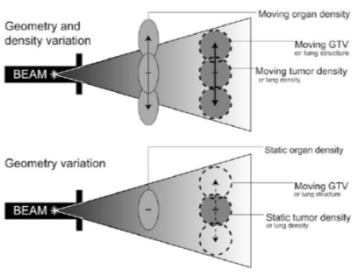
**Tumore polmonare: e' possibile un approccio semplice ma accurato per un planning "formalmente" 4D ??**

**Planning using the MidV dataset to account for respiratory-induced anatomy variation (lung cancer, photon beam)**

- **10 PTs, large tumour motion (median=19 mm)**
- **Conventional and SBRT treatment .**
- **Planning CT: MidV_CT from 4D_CT**
  - **GTV on MidV**
  - **Margin related to patient-specific tumor movement and applied correction strategy**
    - **CRT (offline protocol based on bone anatomy)**
    - **SBRT (online protocol based on tumor position)**

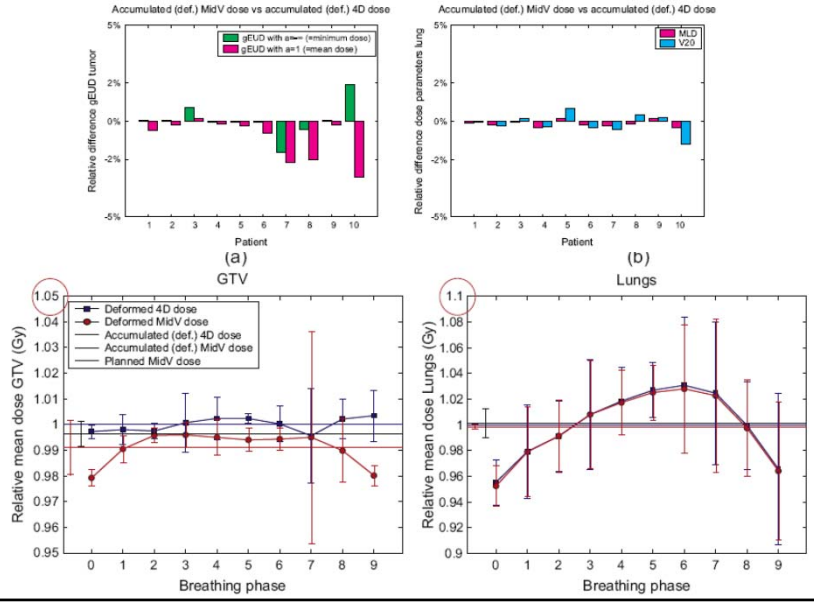
**Mexner et al. IJROBP 2009**

**Planning using the MidV dataset to account for respiratory-induced anatomy variation (lung cancer, photon beam)**

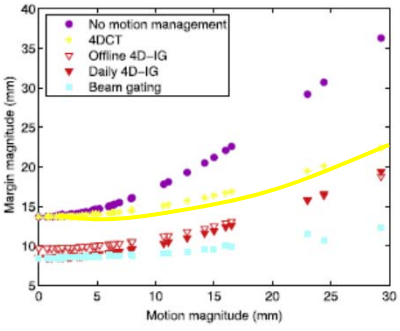



- Geometry variation
  - Plan on MidV
  - Dose **copied** on all other datasets
  - Dose accunulated on MidV
- Geometry+Density variation
  - Plan on MidV
  - Plan **recalculated** on all other datasets
  - Dose accumulated on MidV

## Planning using the MidV dataset IS ACCURATE to account for respiratory-induced anatomy variation (lung cancer, photon beams)




## Lung cancer RT: impact of 4D-CT on margin reduction



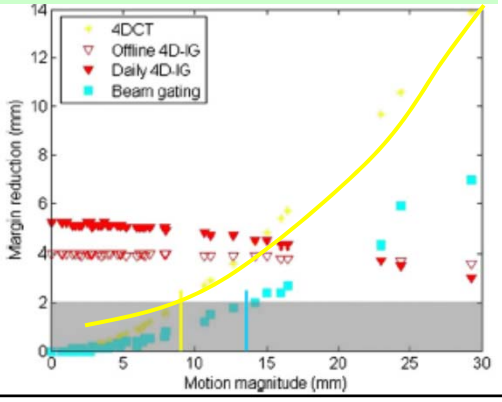

**46 lung Pts, tumor motion 0—30 mm**

**NO-MOTION management:**

- **3D CT + daily set-up on BONY anatomy**

**Motion management:**

- **4DCT (selected phase)**
- **+ 4D-IG (set-up to tumor position)**
- **+ gating**

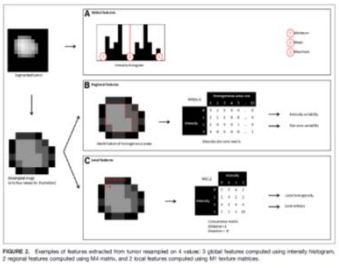


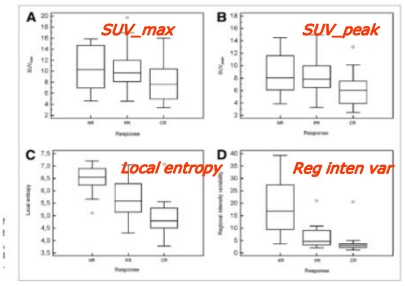

**median margin / % reduction > 2mm**
**4DCT=14 mm (22% red > 2mm)**
**+4D-IG=9-10 mm (100% red > 2mm)**
**+BG=8.6 mm (13% red > 2 mm)**

**Korreman et al. IJROBP 2012**

## Textural features on baseline 18FDG-PET predict reponse to concomitant CRT in esophageal cancer

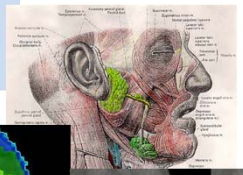
- 41 PTs with esophageal cancer
- 18FDG-PET baseline scan
- Concomitant CHT+ 60Gy
- PTs classified as:
  - non responders (NR)
  - partially responders (PR)
  - complete responders (CR)
- Different indices obtained from pre-treatment PET tumor images (SUV and local/global features)
- Textural features allow for the best stratification in the context of therapy-response prediction

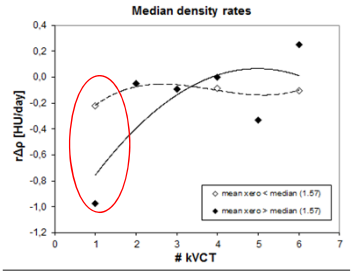


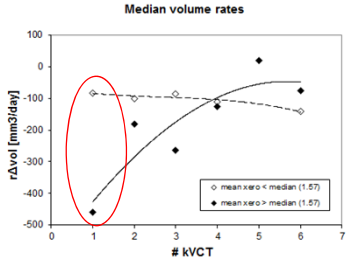



*Tixier at al. J Nucl Med 2011 & 2012*

## Assessing OAR response during RT: ex, parotid ρ/Vol






**rΔρ e rΔvol in the first 2 weeks correlate with mean acute xerostomia score (median value as cut-off)**

**rΔρ e rΔvol** plots for patients with mean score < or >= median value (1.57)

Fiorino et al. 2012, Belli et al. 2013, Scalco et al. 2013

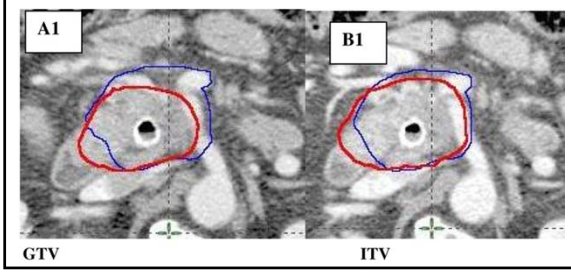
## Local advanced pancreatic tumor. Hypo approach with dose-escalated SIB on infiltrated vessels/pet volume

ITV defined by CE-4D-CT scan: a consistent procedure

-Single phase and 4D procedure have the same intra-observer contouring variability:

- ≈ 25-28% (Percentage difference in delineated volumes)

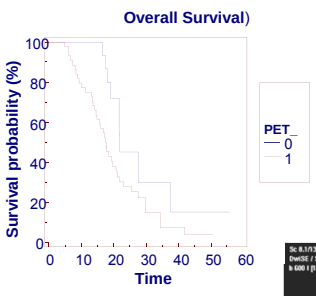
Intra-observer variability in the delineation of GTV (single phase) and ITV (4D procedure)

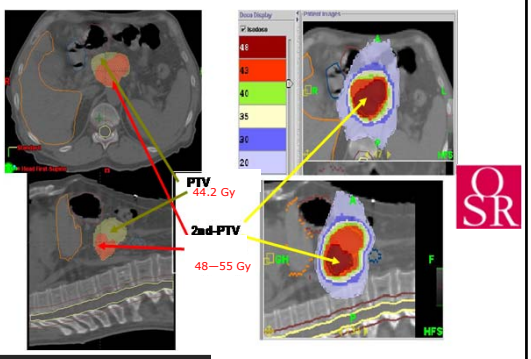


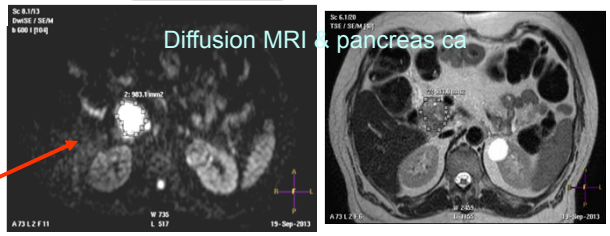

Mancosu et al 2008,
Cattaneo et al 2008, 2013,
Passoni et al 2013

## Local advanced pancreatic tumor. Hypo approach with dose-escalated SIB on infiltrated vessels/pet volumes

4D contrast enhanced CT & PET imaging to define sub volumes to boost




Good outcome, acceptable tox

Inclusion of Diffusion MRI ??

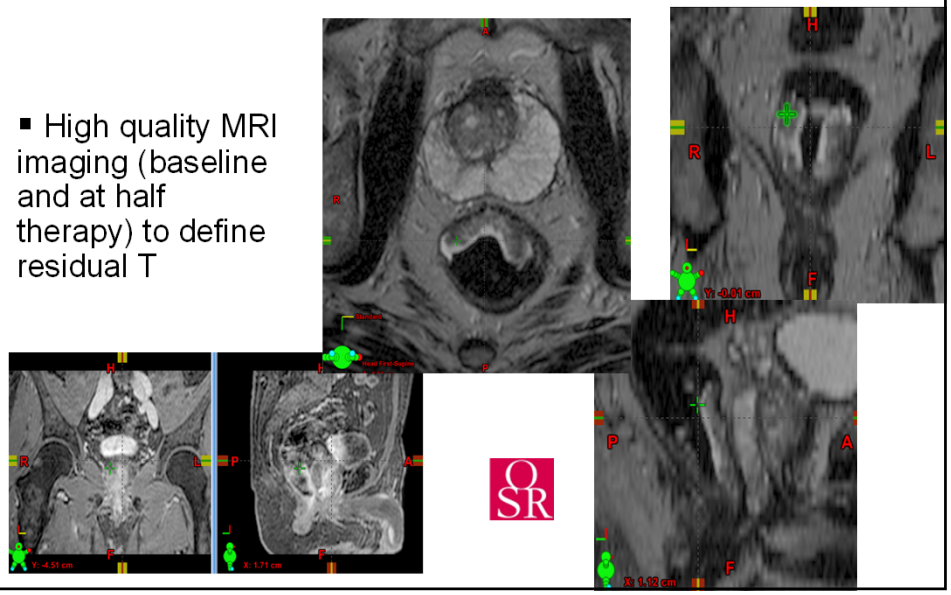
## Neo-adjuvant radiochemo for locally advanced rectal cancer
### *Adaptive concomitant boost @ San Raffaele: rationale*

- The idea: condensing the ART concomitant boost in the last fractions in a moderately hypo scheme because:
- benefit of T shrinkage (and reduced rectal motion (Maggiulli et al. 2012, Raso et al. 2013) minimizing the volume treated at higher dose

  reduces the probability of stopping the treatment due to acute reactions (if the boost in condensed in few fractions)
- focus the boost on the residual cells likely to represent the most resistant part of the tumor

## Adaptive RT rectal cancer @ San Raffaele: building a feasible approach of adaptive boosting…

- High quality MRI imaging (baseline and at half therapy) to define residual T

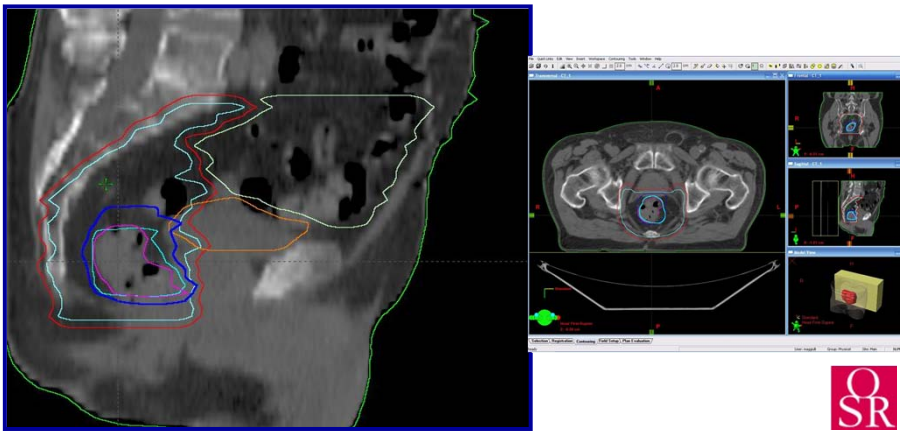


## Adaptive RT rectal cancer @ San Raffaele: evaluating margins ….

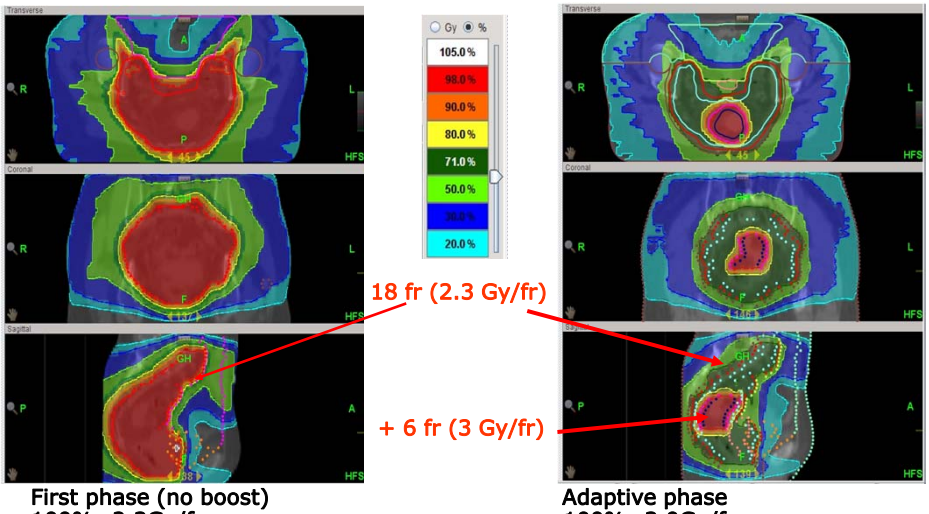
**Rectal envelope first half**

**Rectum on the half therapy CT**

**Rectal envelope second half**



## Adaptive RT rectal cancer @ San Raffaele: Planning




First phase (no boost)
100%=2.3Gy/fr

Adaptive phase
100%=3.0Gy/fr

## Take-home messages

- The continuous integration of advanced imaging modalities (PET, MRI, …) are enlarging the potentials of RT in a "full-patient-driven" OPTIMIZATION !
- The aim of any IMRT+ART approach should be clear, cost-effective, feasible.
- So, DEMANDING but INTERESTING TASKS
- Good LUCK !!!

OSR
Medical Physics DPT
Radiotherapy DPT
Nuclear Medicine DPT

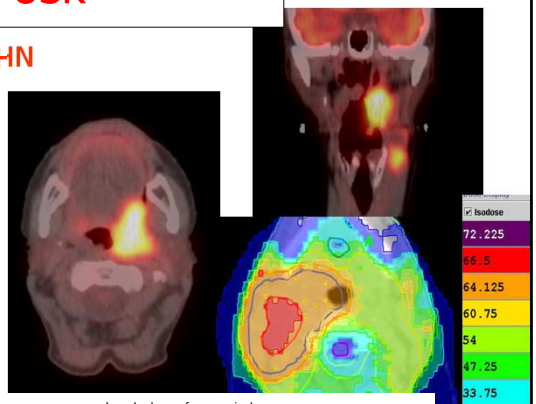
## Esperienza OSR

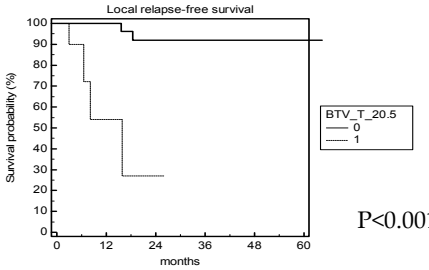
FDG PET & HN

- Simultaneous integrated boost (SIB) technique with Tomotherapy since 2005 (Fiorino et al. 2006, 2007)
- Prescribed dose: 56/66/69 Gy

a) Good outcome with acceptable toxicity (n=63, fup=24m)

b) Initial FDG_PET positive volume is predictive of the response…!




P<0.001

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