# Functional and Molecular Imaging for Radiation Therapy Guidance

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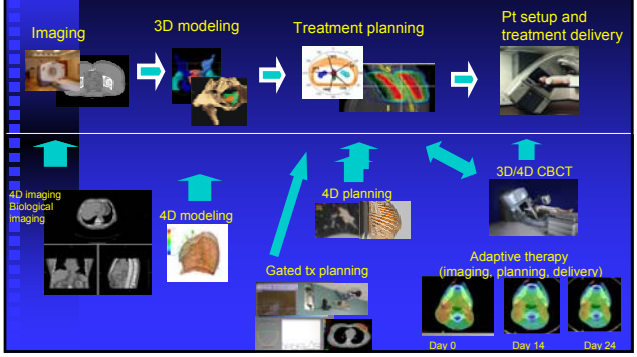
## IGRT Today

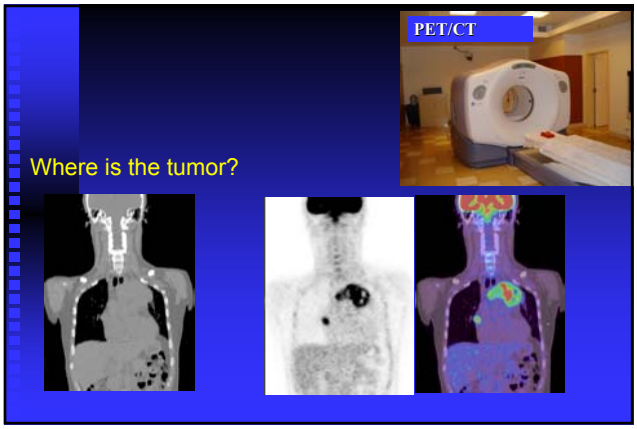



## Targeting in current radiation oncology

Intra-fraction organ movement, in particularly, respiratory motion

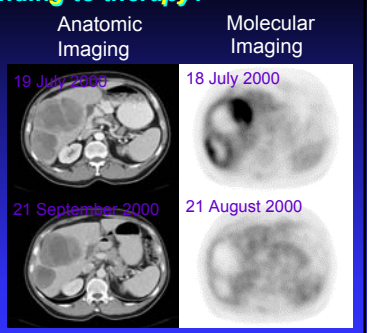
Inter-fraction organ movement

Target volume definition & localization




## *Is tumor responding to therapy?*

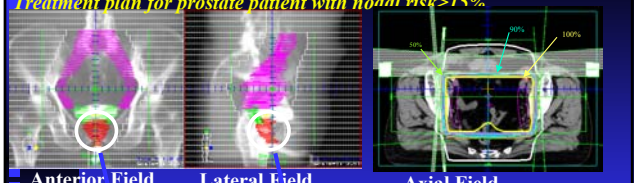
- Tissue Characterization and Classification
- Staging
- Restaging
- Prognosis
- Monitoring Treatment



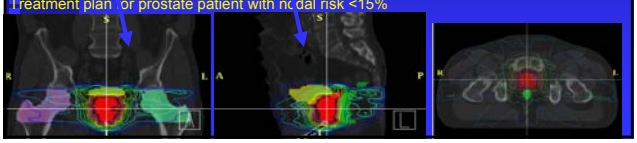

A. Quon

## Pre-treatment staging & planning

*Treatment plan for prostate patient with nodal risk>15%*




Treatment plan for prostate patient with nodal risk <15%

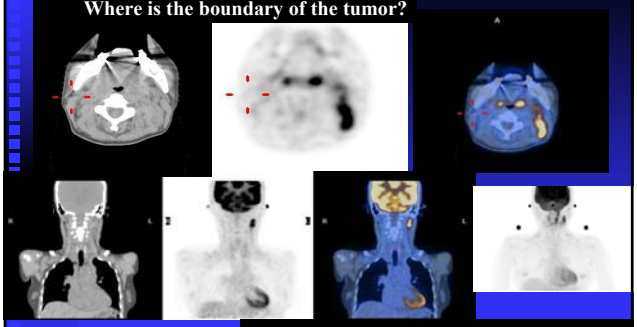


## Shortcomings of Current Radiation Therapy

- Staging and treatment decision-making are based largely on anatomical imaging.
- Tumor volume defined on CT/MRI may often be too small or too large.
- The whole Rx course takes 5-6 weeks and there is no effective tools to distinguish responders from un-responders.
- Detection of recurrence is problematic.
- Spatial biology distribution is not considered

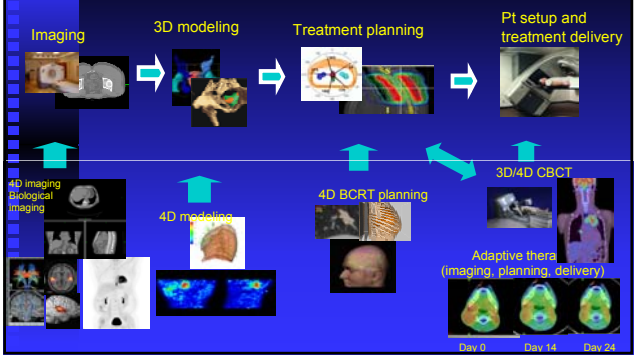
Where is the tumor?

Where is the boundary of the tumor?



What is the biology distribution?

## IGRT Tomorrow - BCRT




- IMRT provides an unprecedented means to produce customized 3D-dose distributions with sub-cm resolution.

- Integration of radiological imaging techniques allows better patient positioning and dose delivery.

- Functional/metabolic imaging modalities are available for noninvasively providing critical needed metabolic and physiological data.

- Molecular imaging techniques are emerging.

## IGRT Tomorrow- BCRT

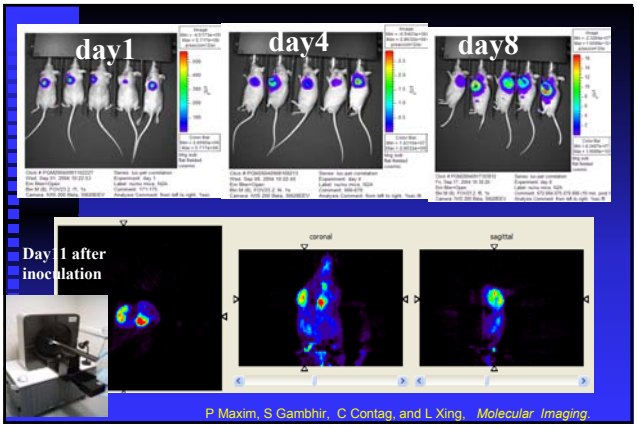
➢ Integration of biological and functional Image.

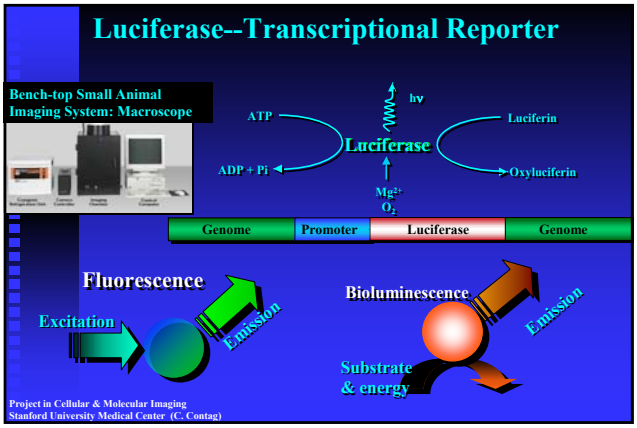
-- Biologically Conformal Radiation Therapy (BCRT)

----to truly individualize radiation therapy

## The Current Imaging Toolbox

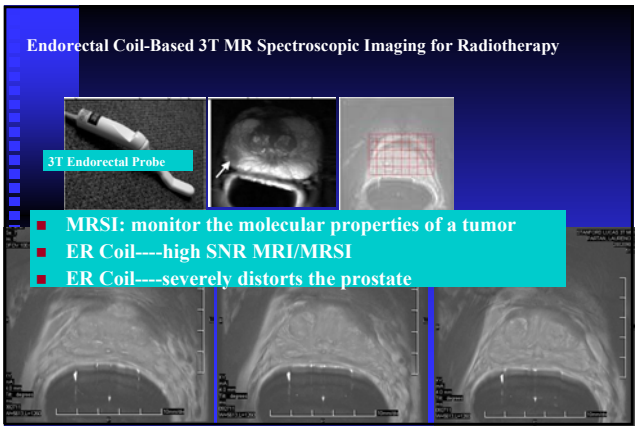
| Method | Minimum Detectable Size (ϕ) | Minimum Detected Cells (n) |
|---|---|---|
| CT | 1~2 mm | 400,000 |
| MRI | 1~2 mm | 400,000 |
| MRSI | 7 mm (~3mm at 3T) | 1,000,000 |
| SPECT | 4~6 mm | 600,000 |
| PET | 3~5 mm | 400,000 |
| HFUS | <1 mm | 100,000 |
| Optics | 0.02 mm | 1000 |




## Clinically available molecular/Functional imaging tools

- MR Spectroscopic Imaging (MRSI)
- Functional MRI, DWI/DTI
- PET, SPECT




## PET and PET/CT

| Topic | Example |
|---|---|
| Characterization of Tissue | Solitary Pulmonary Nodules |
| Staging | Lung Cancer |
| Restaging/Prognosis | Lymphoma/Breast Cancer |
| Monitoring Treatment | GIST, Breast CA, Lymphoma |
| Emerging Applications | XRT planning |

- *Appropriate management decisions starts with accurate staging*
- *PET changes overall management in more than 30% of cases*

*Gambhir, et al 2001*

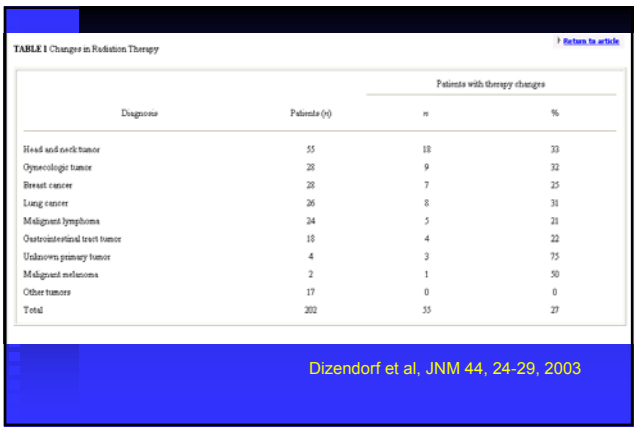


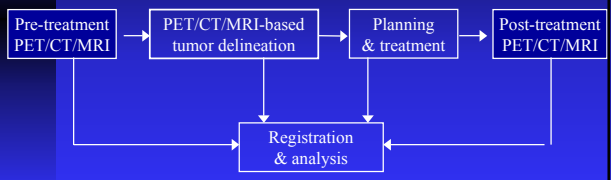
TABLE 1 Changes in Radiation Therapy

| Diagnosis | Patients (*n*) | Patients with therapy changes | |
|---|---|---|---|
| | | *n* | % |
| Head and neck tumor | 55 | 18 | 33 |
| Gynecologic tumor | 28 | 9 | 32 |
| Breast cancer | 28 | 7 | 25 |
| Lung cancer | 26 | 8 | 31 |
| Malignant lymphoma | 24 | 5 | 21 |
| Gastrointestinal tract tumor | 18 | 4 | 22 |
| Unknown primary tumor | 4 | 3 | 75 |
| Malignant melanoma | 2 | 1 | 50 |
| Other tumors | 17 | 0 | 0 |
| Total | 202 | 55 | 27 |

Dizendorf et al, JNM 44, 24-29, 2003

## PET/CT for Radiation Therapy

- delineate target volume
- assess therapeutic response
- distinguish recurrent tumor and radiation necrosis




## Commonly used positron emitters

| Isotope | Half-life (min.) | Production method | Max. range in water (mm) | Application | Production |
|---|---|---|---|---|---|
| $^{11}C$ | 20 | Cyclotron | 1.1 | $^{11}C$-Choline | $^{11}B(p,n)^{11}C$ |
| $^{13}N$ | 10 | Cyclotron | 1.4 | $^{13}N$ ammonia | $^{12}C(p,n)^{13}N$ |
| $^{15}O$ | 2 | Cyclotron | 1.5 | $^{15}O$ water | $^{14}N(d,n)^{15}O$ |
| $^{18}F$ | 110 | Cyclotron | 1.0 | FDG, FLT | $^{18}F(p,pn)^{18}F$ $^{18}O(p,n)^{18}F$ |
| $^{68}Ga$ | 1.1 hr | Generator | 1.7 | | |
| $^{82}Rb$ | 1.3 | Generator | 1.7 | | |

FLT, $^{11}C$-choline, $^{18}F$-choline, Acetate, F-Dopa, Cu-ATSM, F-MISO, F-EF5…

Receptors and peptide-based tracers.

## Proliferation imaging

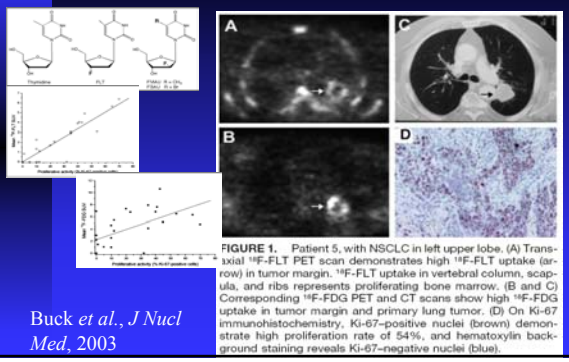
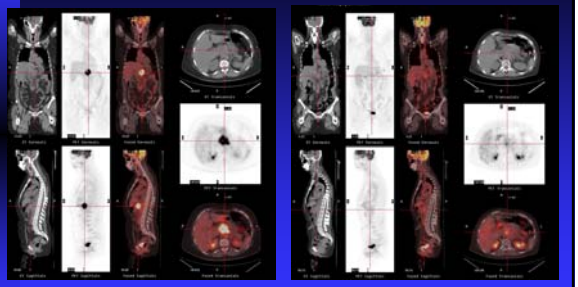
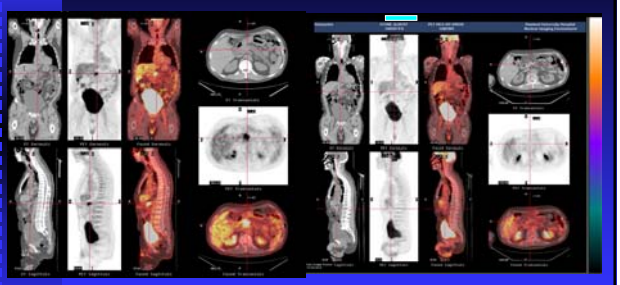



**FIGURE 1.** Patient 5, with NSCLC in left upper lobe. (A) Transaxial $^{18}F$-FLT PET scan demonstrates high $^{18}F$-FLT uptake (arrow) in tumor margin. $^{18}F$-FLT uptake in vertebral column, scapula, and ribs represents proliferating bone marrow. (B and C) Corresponding $^{18}F$-FDG PET and CT scans show high $^{18}F$-FDG uptake in tumor margin and primary lung tumor. (D) On Ki-67 immunohistochemistry, Ki-67–positive nuclei (brown) demonstrate high proliferation rate of 54%, and hematoxylin background staining reveals Ki-67–negative nuclei (blue).

Buck *et al.*, *J Nucl Med*, 2003

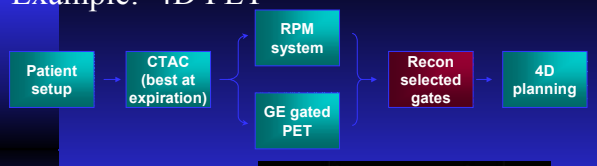




## Functional Image-Guided IMRT

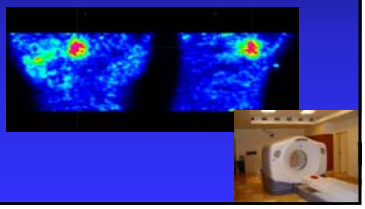
- **What needs to be done?**
  - **Reliable imaging tools.**
  - **Integration---network transfer of functional image files, file format conversion, image fusion/deformable image registration….**
  - **Image fusion.**
  - **Inverse treatment planning.**
  - **Quality assurance .**
  - **Clinical study of the efficacy.**

# Example: 4D PET




If bin size = Δt, then in each respiratory cycle:

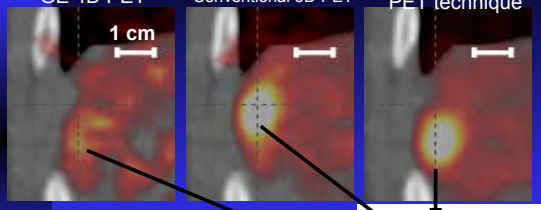
Bin 1 accumulates events from [0, Δt]
Bin 2 accumulates events from [Δt, 2Δt]
Bin 3 accumulates events from [2Δt, 3Δt]
.
.
.
Bin N accumulates events from [(N-1)Δt, NΔt]





A Liver Cancer patient

GE 4D PET | Conventional 3D PET | Stanford new 4D PET technique

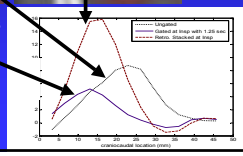



3D PET --- the lesion in the ungated image is elongated, and mislocalized superiorly by ~1 cm.

GET PET – location is right but signal is week.

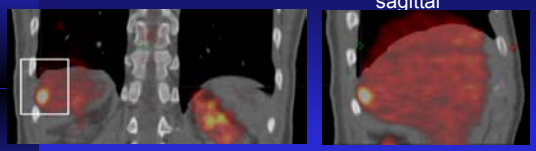
RS 4D PET – location and signal are great☺.

3D PET give wrong location and wrong volume



# RS 4D PET imaging technique

sagittal



Stanford 4D PET image at end-inspiration. The lesion has clearly emerged from the background activity at the end-inspiration location.

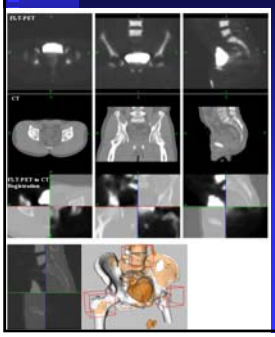
(B. Thorndyke, E. Schreibmann, A. Koogn, and L. Xing, Med Phys, 2006).

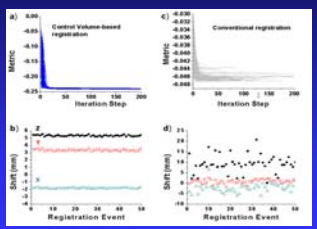
# Functional Image-Guided IMRT

- What needs to be done?
  - Reliable imaging tools.
  - Inverse treatment planning.
  - Quality assurance .

# Image Registration

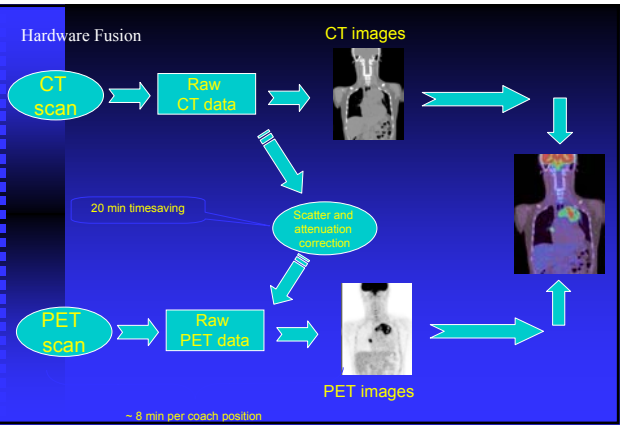
➢ Automated registration based on control volume(s).





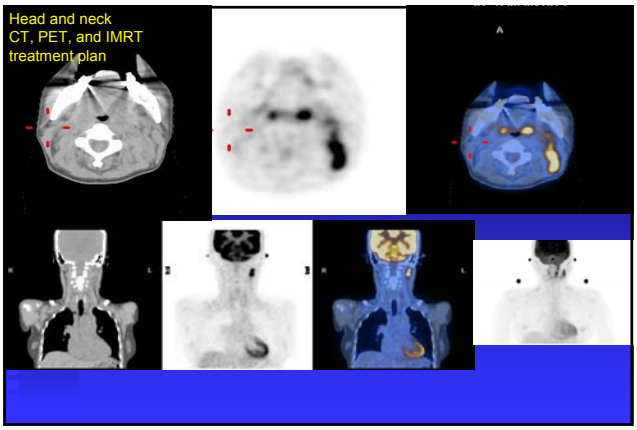

Schreibmann and Xing, Med. Phys., 2006.

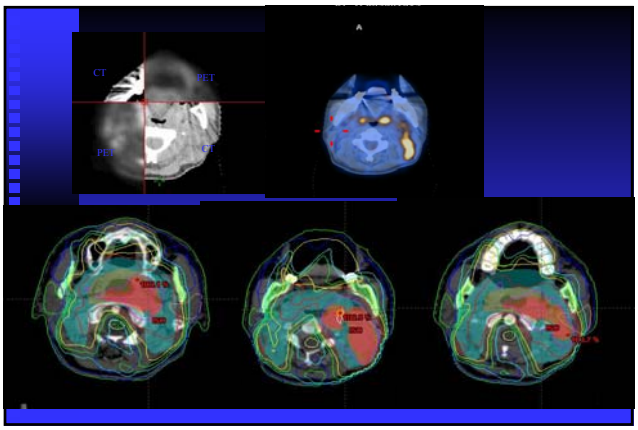
Hardware Fusion

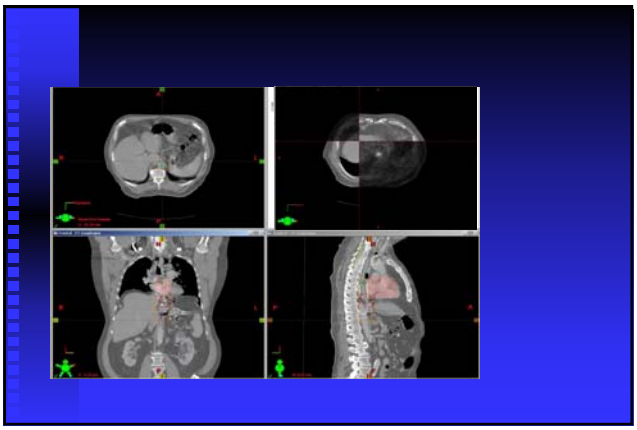


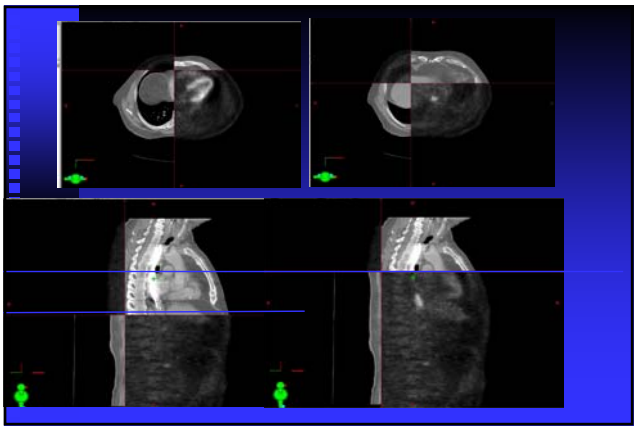

~ 8 min per coach position

Head and neck
CT, PET, and IMRT
treatment plan

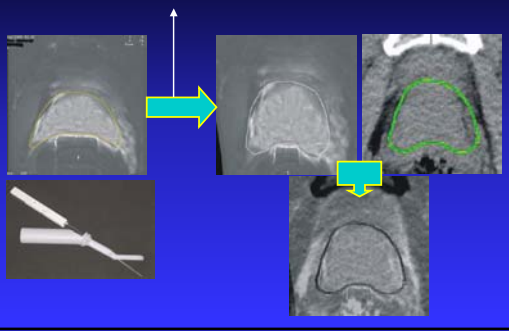




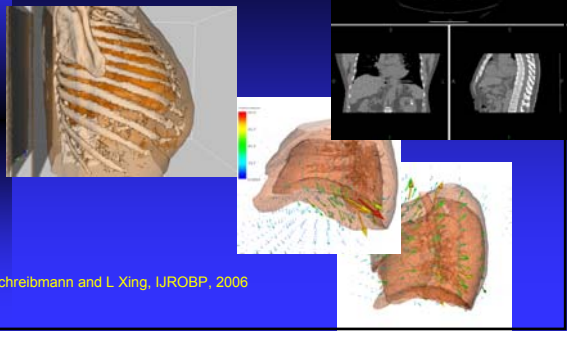





- Deformable image registration



4D Image Registration



E. Schreibmann and L Xing, IJROBP, 2006

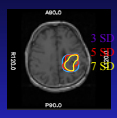
## Functional Image-Guided IMRT

- What needs to be done?
  - Reliable imaging tools.
  - Image fusion.
  - Quality assurance .

## Biological image based inverse treatment planning

PET/MRI/MRSI

Post-scan data processing

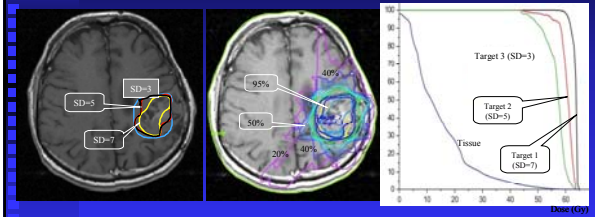



**Quantify metabolism**

Inverse planning

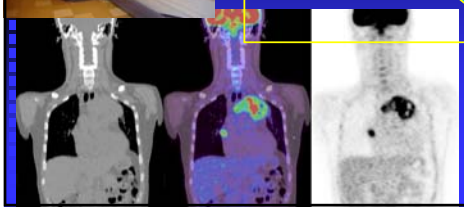
- Prescription
- Beam orientation/profile optimization
- Fine-tune regional doses
- Plan review
- MLC leaf sequencing

## IMRT Plan Incorporating MRSI data




L. Xing et al, PMB 47, 3567-3578, 2002 .

## Biologically Conformal Radiation Therapy

## Prescription for molecular/functional image guided IMRT

$$TCP_i = \exp[-\rho_{0i} v_i \exp(-\alpha_i D_i + \gamma_i \Delta T)]$$

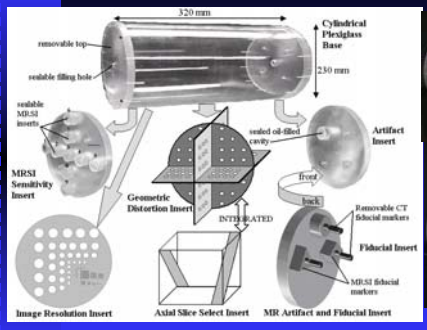
$$D_i = \frac{\alpha_r}{\alpha_i} D_r - \frac{1}{\alpha_i}(\gamma_r - \gamma_i)\Delta T - \frac{1}{\alpha_i}\ln\left(\frac{\alpha_r \rho_{0r}}{\alpha_i \rho_{0i}}\right)$$

Yang Y and Xing L, Med. Phys. 2005.

## Functional Image-Guided IMRT

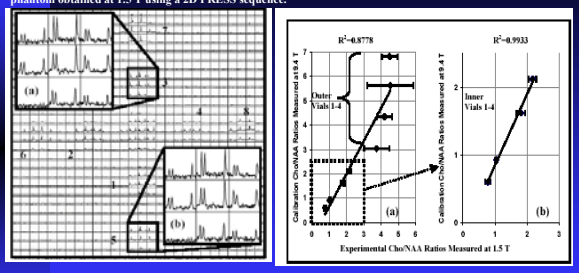
- What needs to be done?
  - Reliable imaging tools.
  - Image fusion.
  - Inverse treatment planning.
  - Quality assurance .

## Quality Assurance



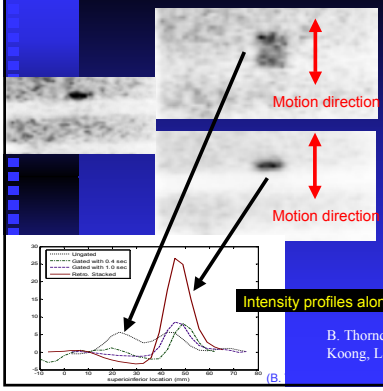

S. Hunjan, D. Kim, A. Adalsteinsson, D. Spielman, L. Xing, IJROBP 57, *1159-1173, 2003*

**Relationship between the Cho/NAA ratios of the calibration solutions obtained at 9.4 T versus the calibration-solution-filled vials inside the phantom obtained at 1.5 T using a 2D PRESS sequence.**




S. Hunjan, D. Kim, A. Adalsteinsson, D. Spielman, L. Xing, IJROBP 57, *1159-1173, 2003*

## 4D PET Image Enhancement - Phantom Validation




3D PET

4D PET (after post-acquisition data processing using our new algorithm)

Intensity profiles along the motion direction

B. Thorndyke, E. Schreibmann, A. Koong, L Xing, Med. Phys. 2006

## Functional Image-Guided IMRT

- **What needs to be done?**
  - **Reliable imaging tools.**
  - **Image fusion.**
  - **Inverse treatment planning.**
  - **Quality assurance .**
  - **A lot of research!**

## In Vivo Small Animal Imaging Modalities

Anatomic | Physiologic | Metabolic

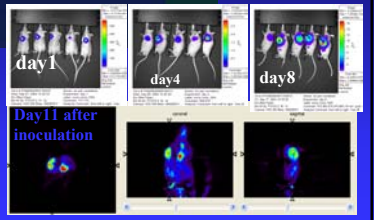
optical imaging

x-ray CT | PET/SPECT

MRI | MR Spectroscopy

fMRI

ultrasound


P Maxim, S Gambhir, C Contag, and L Xing, *Molecular Imaging*, 2004

## Summary

Functional/molecular imaging is emerging.

Next Generation Radiation Therapy
Integration of functional & molecular imaging
Biologically Conformal IMRT
----to truly individualize Rx

Reliable imaging tool, registration, inverse planning, QA, research.

# ACKNOWLEDGEMENTS

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