MULTI-MODAL IMAGE INTEGRATION

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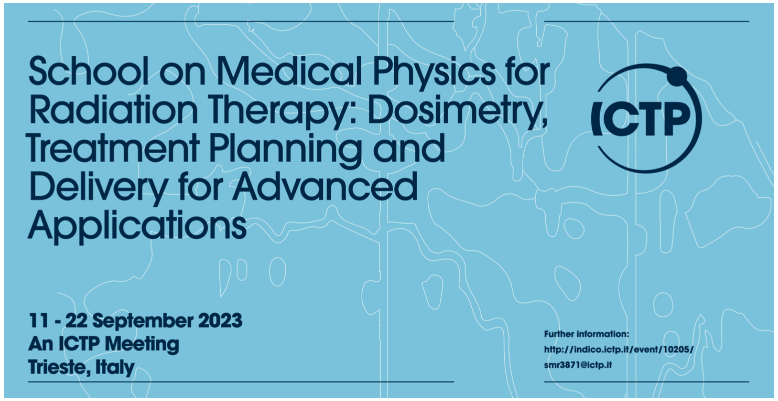


MULTIMODAL IMAGE INTEGRATION vs. REGISTRATION

- **image integration** = the use of two or more image sets in the process of (i.e.) treatment planning

- **image registration** = the process of making two or more image sets spatially coherent to each other

- **image fusion** = the simultaneous visualization of two or more image sets, previously coregistered

IMAGING MODALITIES RELEVANT TO TREATMENT PLANNING

- **computed tomography (CT)**
  - basic modality for treatment planning
- **magnetic resonance imaging (MRI)**
  - multimodality imaging technique
  - morphological and functional information
- **PET-CT**
  - low resolution datasets
  - CT inherent to modality – easy spatial reference
- **ultrasound (US)**
- **emerging modalities** (PET-MR etc.)

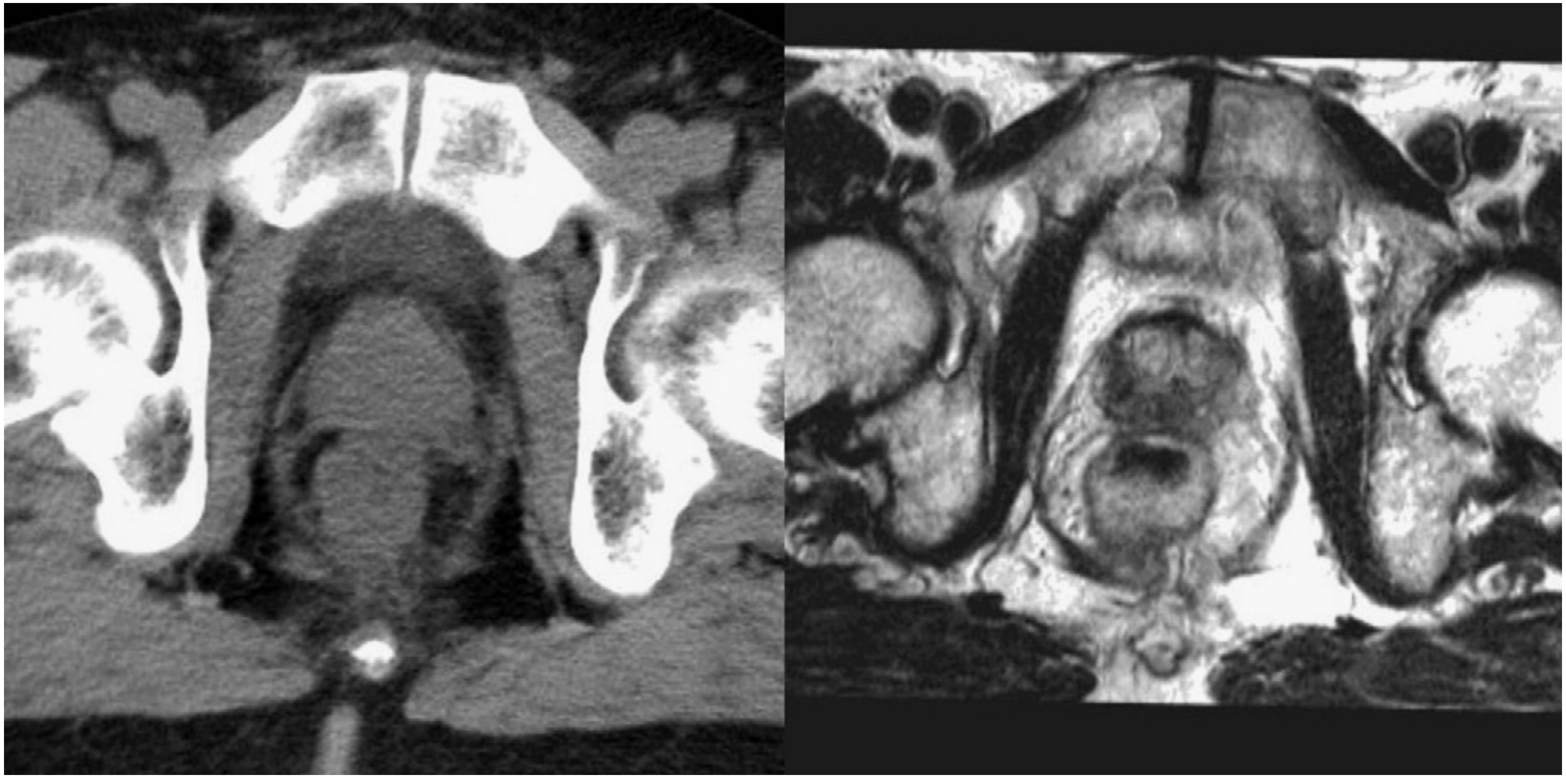
THE CENTRAL ROLE OF CT IN TREATMENT PLANNING

- CT is the tomographic modality that offers the best **spatial accuracy** (freedom from significant distortion etc.)

- CT information can be directly transformed into a **map of attenuation coefficients** => useful in dose calculation

- modern in-room verification systems are based on **x-ray transmission imaging** (e.g. CBCT) => easily registered to CT

MR FOR TREATMENT PLANNING



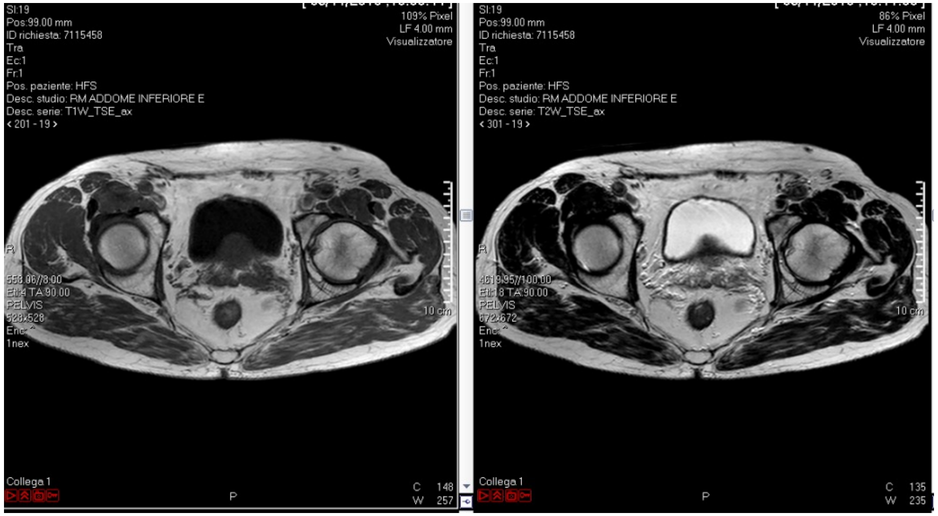
- example: comparison between CT and MR – prostate
- better visualization of soft tissue
- no direct correspondence between "gray levels" => may complicate automatic image registration

MORPHOLOGICAL T1- AND T2-BASED IMAGING

- **T1 and T2** weighting corresponds to imaging with different “modalities”

- **T1** enhances **muscle-fat** - **T2** enhances **water** (fluids)

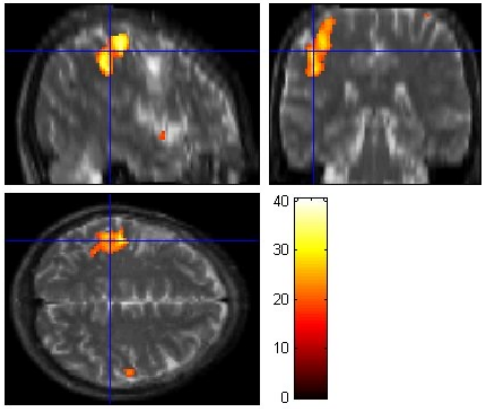
- Paramagnetic **contrast agents** have more effect on **T1-weighted** images

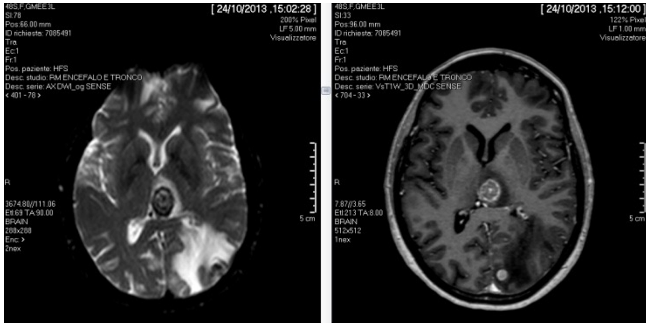


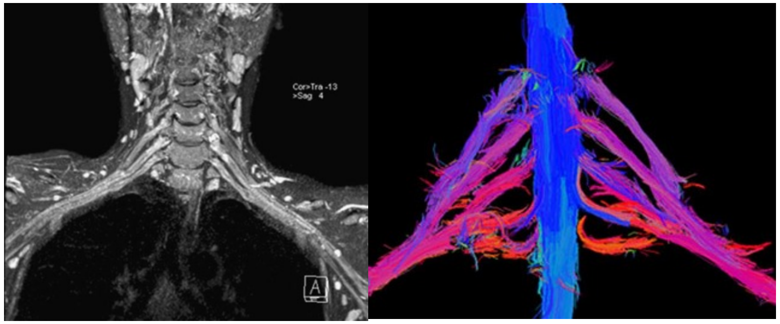
left: T1-weighted MR image
right: T2-weighted MR image

FUNCTIONAL INFORMATION FROM MRI

- MRI can provide valuable **functional information** by means of:
  - *diffusion-weighted imaging (**DWI**) – including maps of apparent diffusion coefficient (**ADC**) and diffusion tensor imaging (**DTI**) – tractography*
  - ***fMRI** based on the **BOLD** effect*
  - *arterial spin labeling (**ASL**)*
  - *…*







FUNCTIONAL INFORMATION FROM MRI

- functional MRI is characterized by **low spatial resolution (low SNR)**

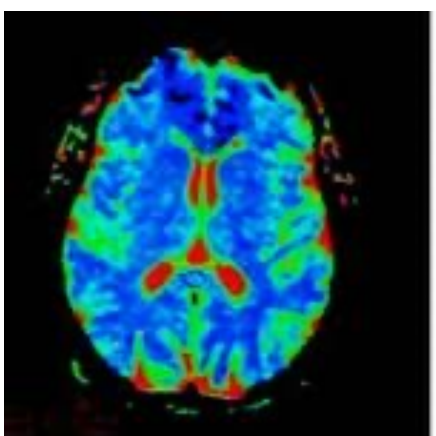
- fMRI is often reported on **anatomical atlases** for reference

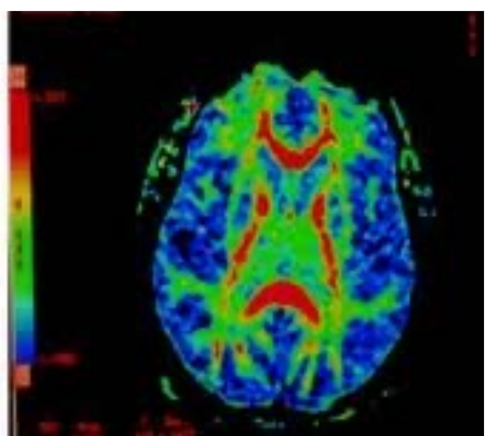
=> registration to CT might be difficult because of **poor “common information”**

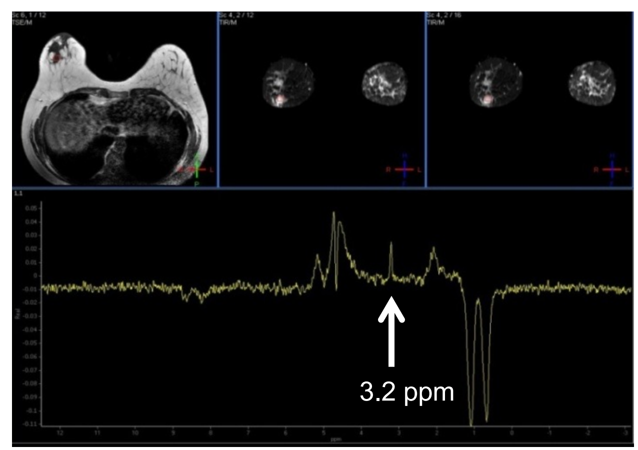
MULTIPARAMETRIC MR IMAGING

- Special MRI modalities such as **DWI** (ADC) and **spectroscopy** may be integrated for diagnostic purposes (multi-parametric imaging)

- Multi-parametric datasets are **usually not employed in the treatment planning process**; special attention needed

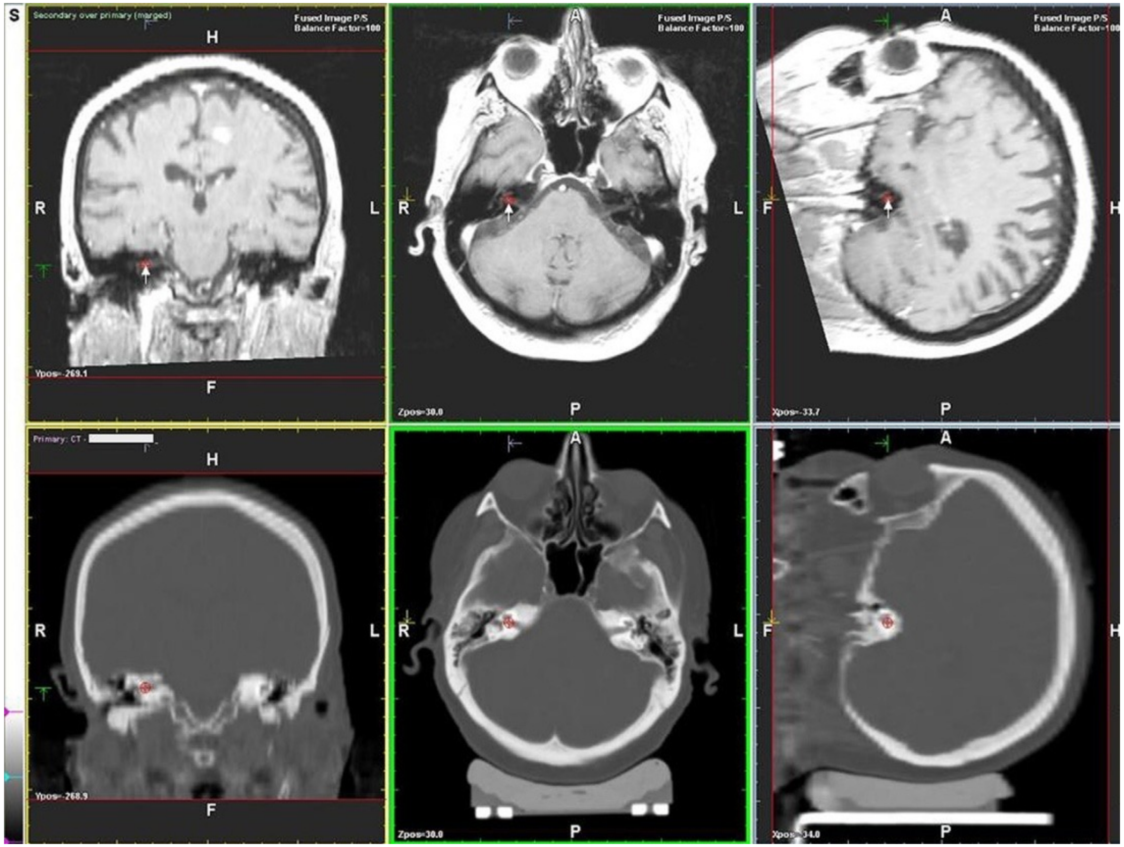






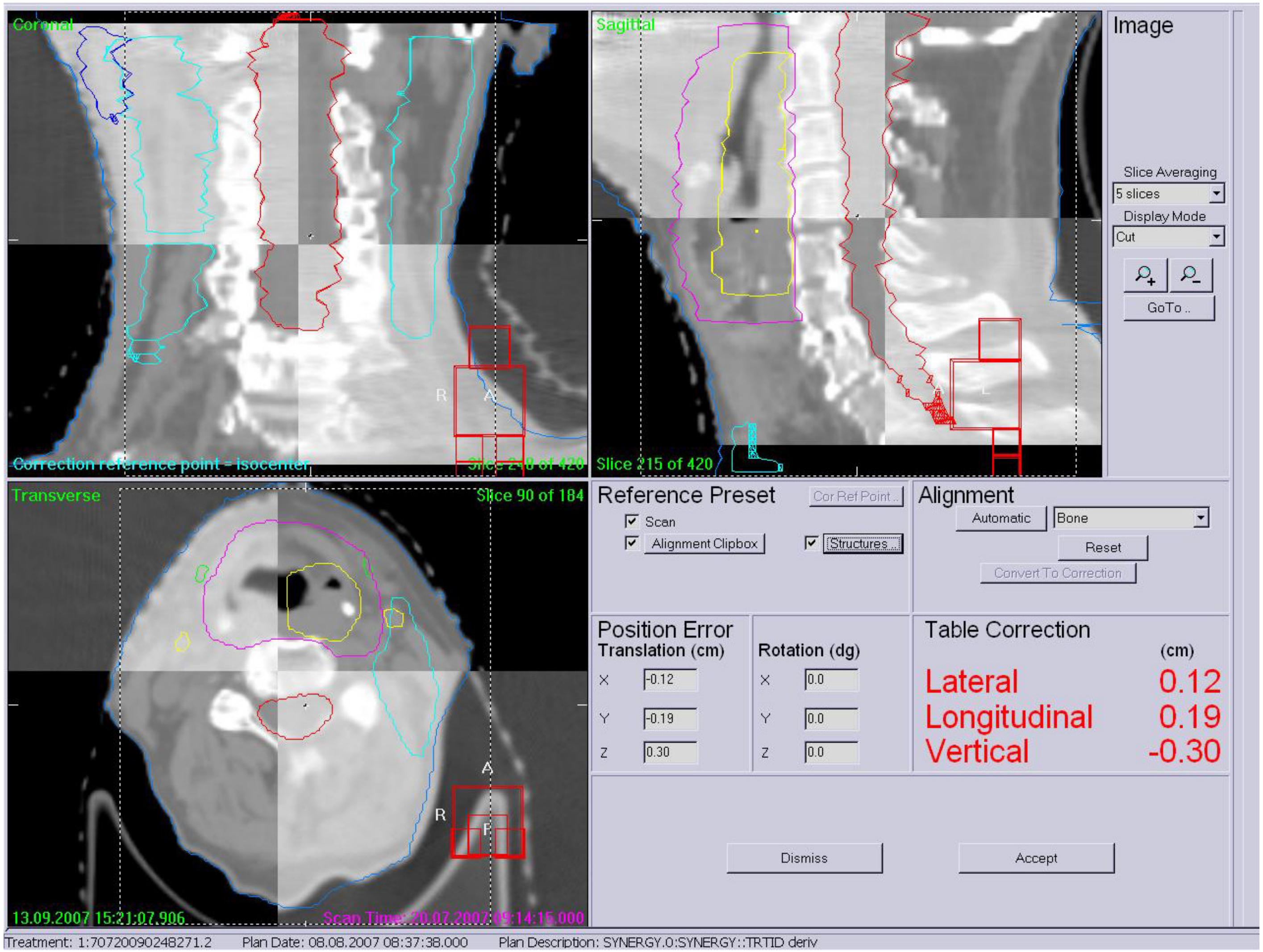
COREGISTRATION BETWEEN MRI AND CT

- Strictly **rigid transformation** in the brain
- 3 translations+3 rotations => 6 parameters



- Diagnostic MRI is usually **rotated around the L-R axis** compared to CT
- **Correction needed** – might not be evident on axial orientation
- Inferior regions might introduce **deformations**

COREGISTRATION BETWEEN MRI AND CT



COREGISTRATION BETWEEN MRI AND CT

- Use of “**clip-boxes**” in case of deformations to disregard in the registration process

- Commercially available treatment planning systems and 3rd party software **may offer** this functionality

- Privilege the anatomical region that has to be coregistered – leave any uncontrolled region free

COREGISTRATION BETWEEN MRI AND CT

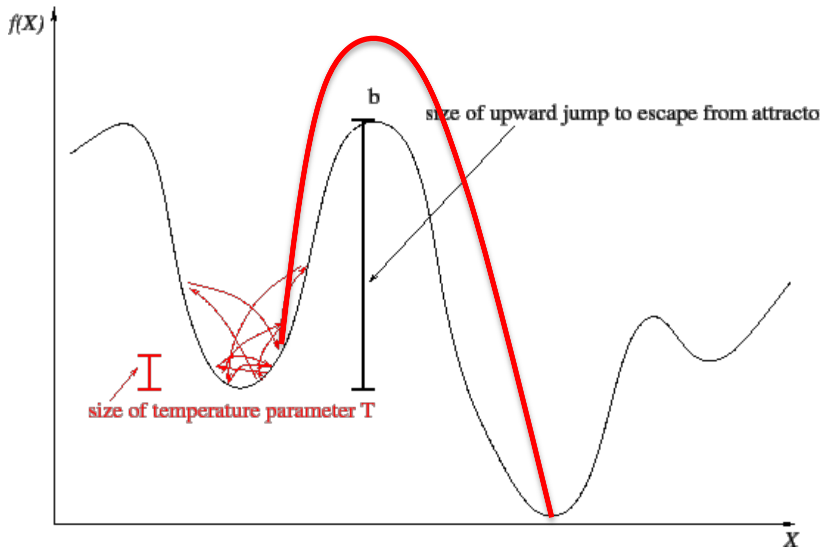
- Obtaining **similar (consistent) initial orientation** is often essential even in case of automatic transformation – robustness of algorithms to different initial orientation is an issue in general

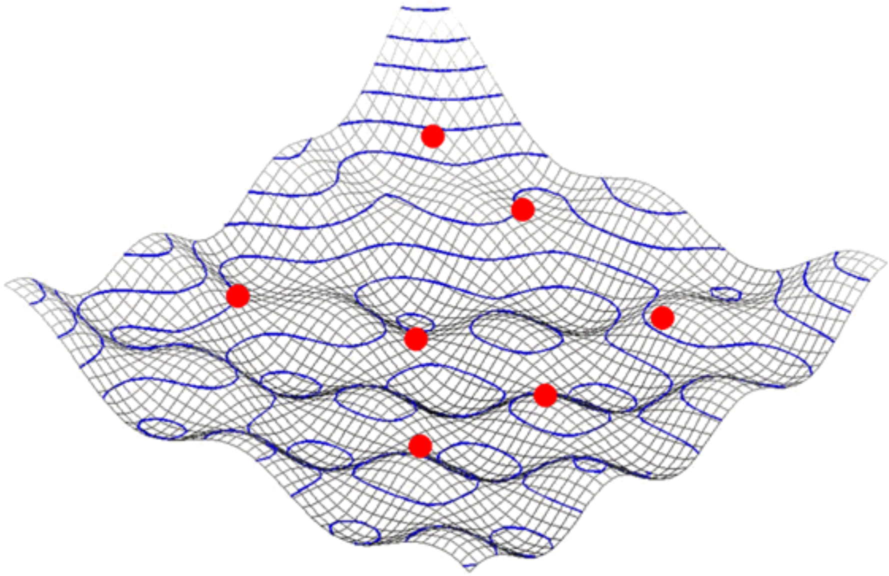
- Use of **patient positioning devices** recommended in case of multimodality imaging – example: PET-to-CT

- Pay attention to **MR compatibility - safety!**

OPTIMIZATION: SEARCH FOR GLOBAL MINIMUM

optimization: *simulated annealing* - multiresolution





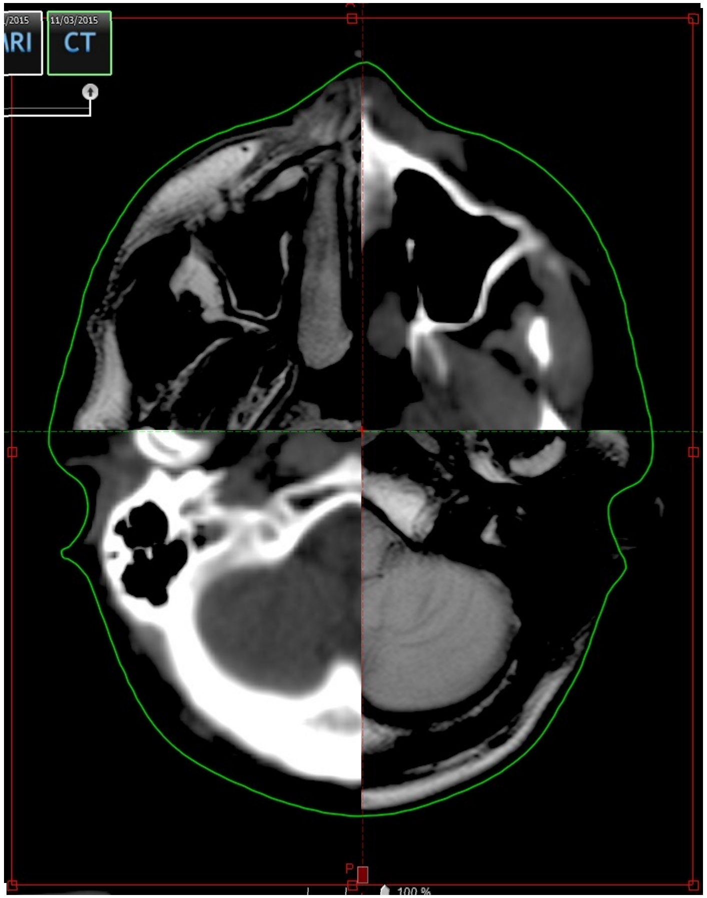
"big steps" necessary to find global minimum of the cost function

multiresolution approach: easier to find global minimum but starting situation still important

COREGISTRATION BETWEEN MRI AND CT

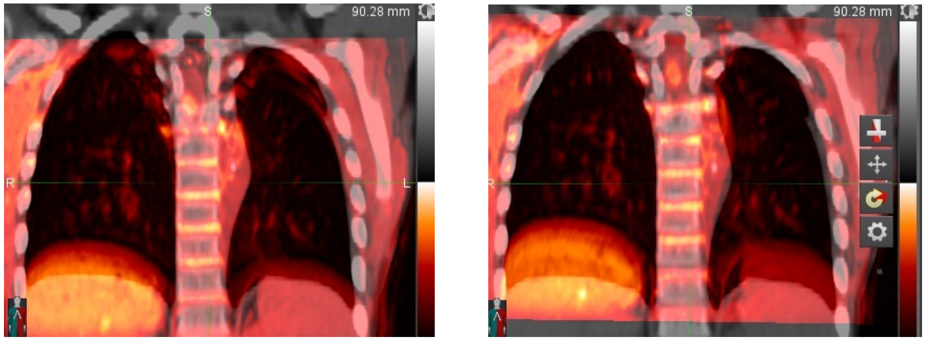
- example of (mild) **non-convergence** in iterative steps

- importance of correct **starting position**



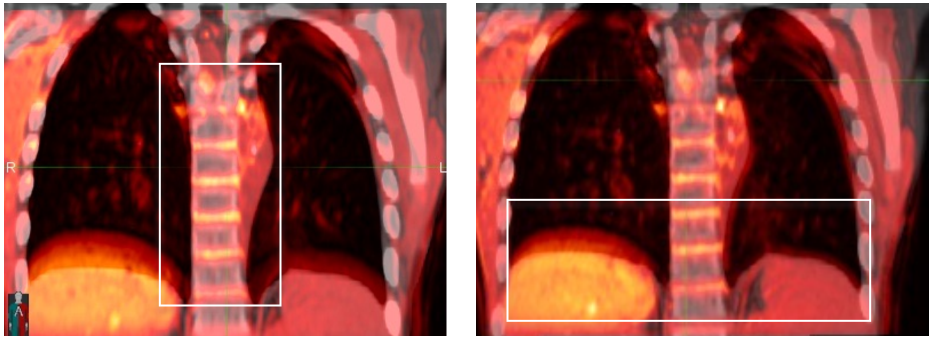
POSSIBLE ERRORS DUE TO LOCAL MINIMA

- example of (severe) **poor robustness** due to anatomical symmetry or moving structures



wrong matching of vertebrae (left)

- modern implementations are generally robust but **attention is necessary**



clipboxes used to limit registration to selected regions

PET-CT FOR TREATMENT PLANNING

- ^{18}**F-FDG PET-CT** imaging is increasingly growing since the introduction of clinical PET-CT scanners (ca. 2000)

- Applications to Radiation Oncology**: PET-based volumes of reference** (BTV=biological target volume)

- Clinical decisions (including “BTV” delineation) generally based on the **Standardized Uptake Volume (SUV)**

PET-CT FOR TREATMENT PLANNING

$$SUV = \frac{c(t)}{A(t)} \cdot bw$$

c = activity concentration (MBq/kg), A = injected activity (MBq), bw=body weight (kg)

- Importance of **standardization** (patient weight, uptake time, injected activity and correction for decay in the uptake time …)

- **Lesion motion** might have negative (even destructive) effects on SUV quantification (see specific module)

PET-CT FOR TREATMENT PLANNING

- Use of SUV to define biological volumes of reference suffers from **several limitations**

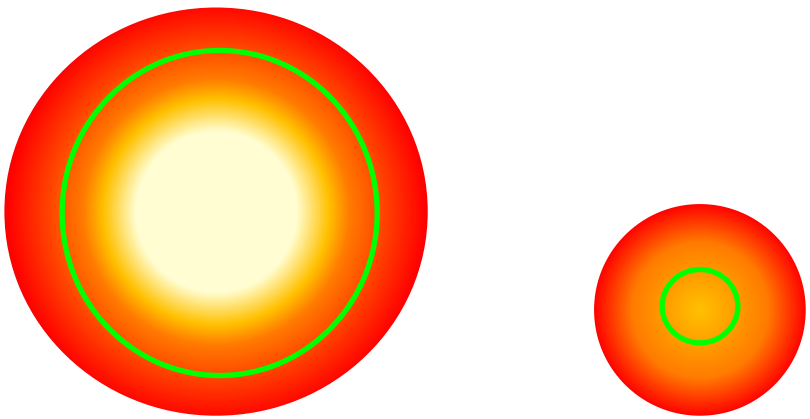
- **Fixed threshold** (e.g. 2.2): different behaviour for small and large lesions

- **Percentage of SUV_{max}**: underestimation in case of inhomogeneous uptake and reconstruction artifacts (e.g. Gibbs artifact in resolution-modeling reconstruction - PSF)

- **Tumor motion** is an additional bias

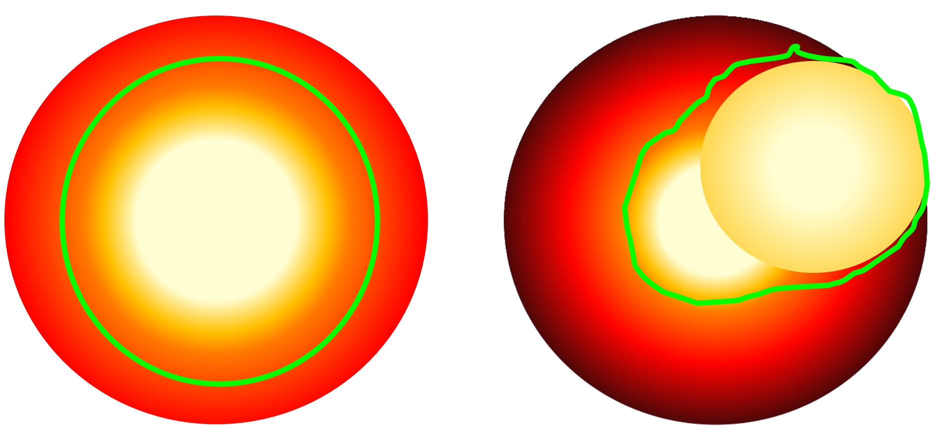
PET-CT FOR TREATMENT PLANNING

- threshold-based contouring (e.g. SUV=2.2)



- small lesions might be underestimated due to small SUV values – large lesions might be overestimated

- percentage-based contouring (e.g. 40% of SUV_{max})



- inhomogeneous lesions tend to be underestimated because of high SUV spots

PET-CT FOR TREATMENT PLANNING

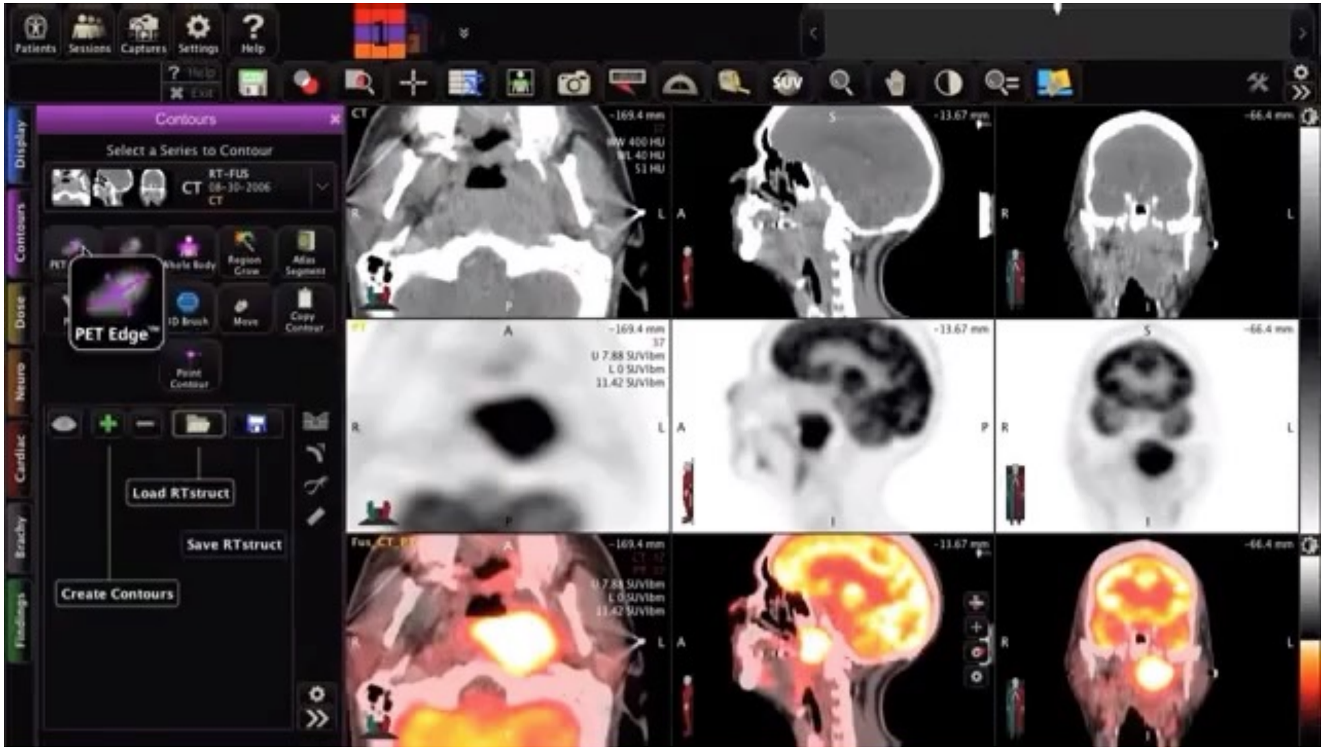
- more refined algorithms are based e.g. on the maximum gradient (gradient-based) or on *object-recognition* or *classification* algorithms

- **there is no recognized "best-in-class" algorithm so far** – a **critical approach** is always necessary when using commercially-available systems

- new algorithms might be more robust with respect to motion artifacts etc. – more research needed

PET-CT FOR TREATMENT PLANNING

- example of gradient-based algorithm



PET-CT REGISTRATION TO CT

- PET-CT has an **inherent CT dataset** that might be used for treatment planning if the required parameters and conditions are used

- PET-CT can be **registered to a different (setup) CT** – usually through **CT-CT (intra-modality)** registration whose transformation is then applied to the PET dataset

- Multi-modality PET-to-CT registration is **feasible but should be avoided** (poor "common information")

IMAGE REGISTRATION - METHODS

- **Spatial coherence** between different imaging modalities used for treatment planning may be a key factor for treatment success

- **Manual registration** methods must be **avoided** when co-registering 3D datasets

- **Automatic methods** are implemented on modern treatment planning systems for **rigid registration**

- **Deformable registration** is seldom implemented and requires careful evaluation of results – however necessary for adaptive strategies (dose accumulation)

IMAGE REGISTRATION – transformation types

- **Rigid registration** – described by 6 parameters
  - three translations and three rotations corresponding to the principal axes in 3D

- **Deformable registration – affine** – 12 parameters
  - 3 translations + 3 rotations + 3 scaling f. + 3 shear factors

- **Deformable registration – local**
  - locally rigid registration – free to deform on a large scale
  - B-splines (B-cubic-splines)
  - locally affine
  - biomechanical models (finite elements method - FEM)
  - elastic or visco-elastic models
  - …

STRUCTURE OF A (DEFORMABLE) REGISTRATION ALGORITHM

$$\widehat{T} = \arg_T \max(sim(I_{Ref}, I_{fl} \circ T) + \lambda Reg(T))$$

- *similarity measure*

- *regularization term (deformable only)*

- similarity measures vary as a function of the nature of co-registration (intramodality, multimodality …)

- the regularization term charges a penalty on improbable transformations

SIMILARITY MEASURES

- Least-squares distance (set of **fiducial points**)

- Least-squares distance (**surfaces**)

- Intra-modality problem (e.g. CT-to-CT): **cross-correlation** (or mutual information, see below)

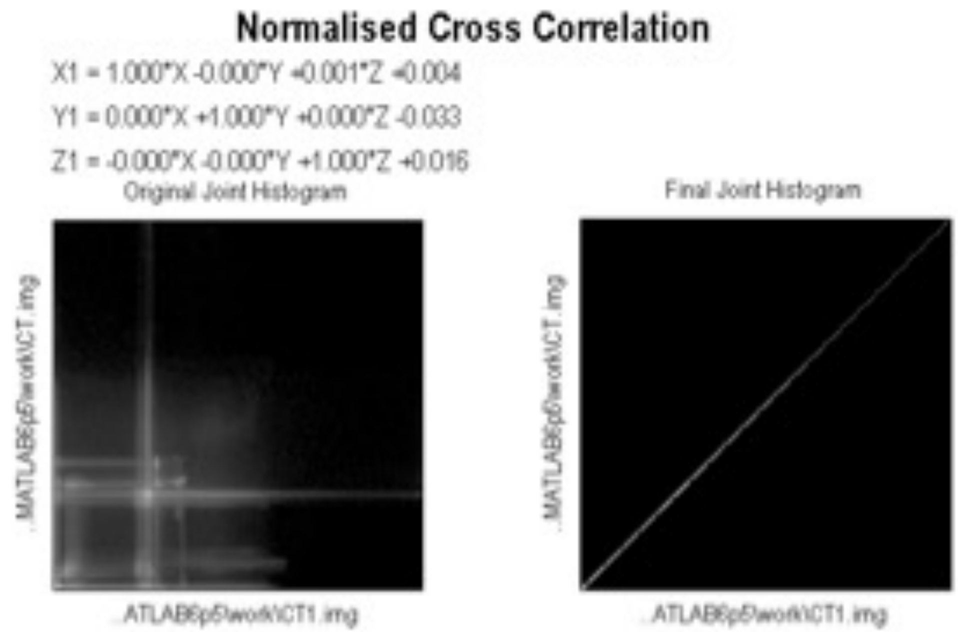
- Multimodality problem (e.g. MR-to-CT): maximization of the **mutual information** index/ **normalized mutual information (NMI)**

- ...

SIMILARITY MEASURE

- **cross correlation**

  - fast and robust method
  - only intramodality or "similar" (e.g. CT – CBCT)



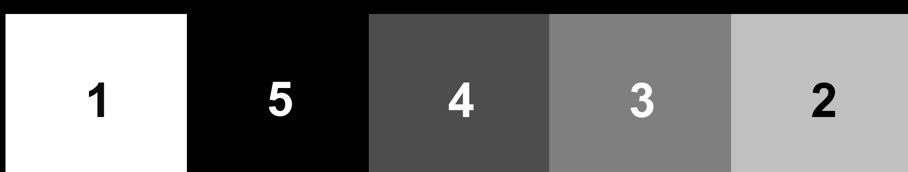
$$R = \frac{\sum_{(i,j)\in T} (I_{fl}(i,j) - \bar{I}_{fl})(I_{ref}(i,j) - \bar{I}_{ref})}{\sqrt{\sum_{(i,j)\in T} (I_{fl}(i,j) - \bar{I}_{fl})^2} \sqrt{\sum_{(i,j)\in T} (I_{ref}(i,j) - \bar{I}_{ref})^2}}$$

IMAGE ENTROPY (INFORMATION)

$$H = \sum_i p_i \log \frac{1}{p_i}$$

p(3)=1

$\Rightarrow$ **H = 0** “PREDICTABLE” MESSAGE – no information added at each step



p(1)=0.2 p(2)=0.2 p(3)=0.2 p(4)=0.2 p(5)=0.2

$\Rightarrow$ **H = 1.61**

“UNPREDICTABLE” MESSAGE – new information added at each step

p(1)=0.2 p(3)=0.6 p(5)=0.2

$\Rightarrow$ **H = 0.95**

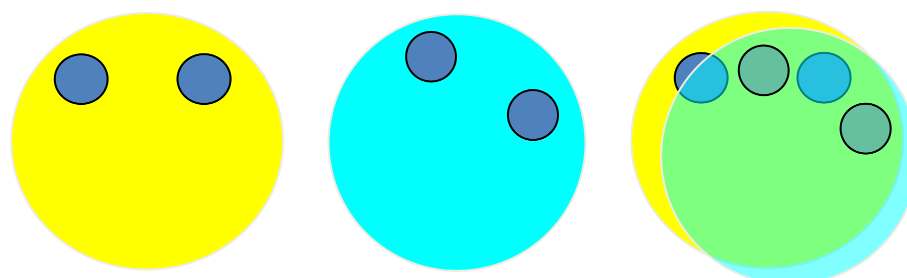
INTERMEDIATE CASE

The MUTUAL INFORMATION index

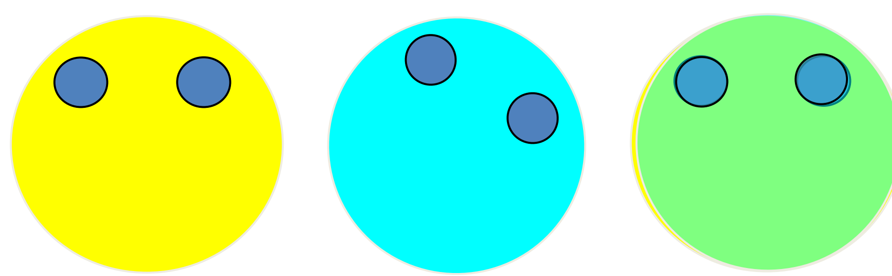
Subtraction of the "joint entropy" ("false" information)
=> maximization of the mutual information index

$$I(A,B) = H(A) + H(B) - H(A,B)$$

NON-REGISTERED IMAGES:



REGISTERED IMAGES:



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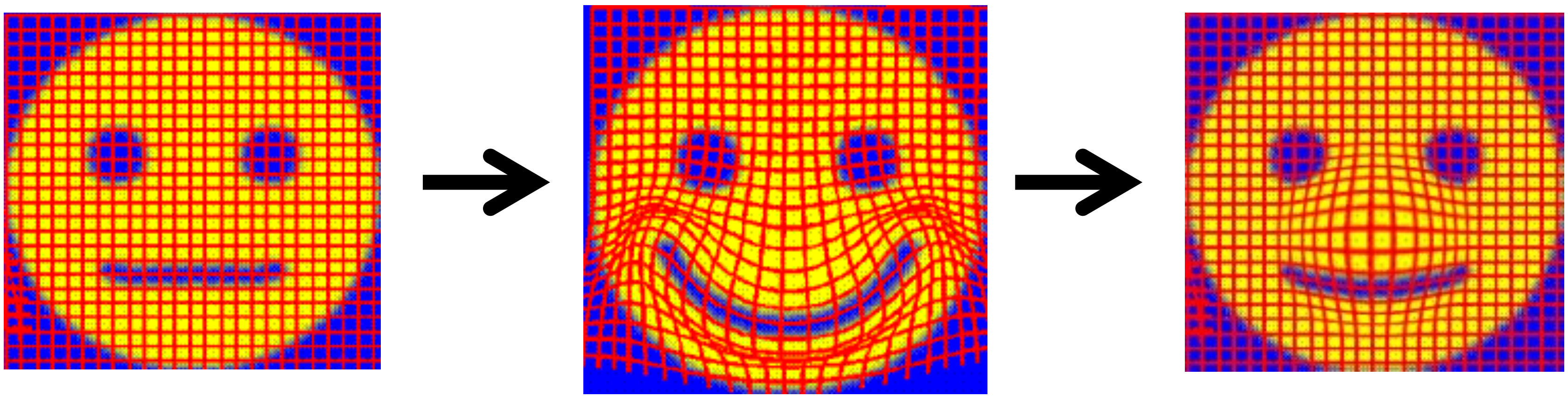
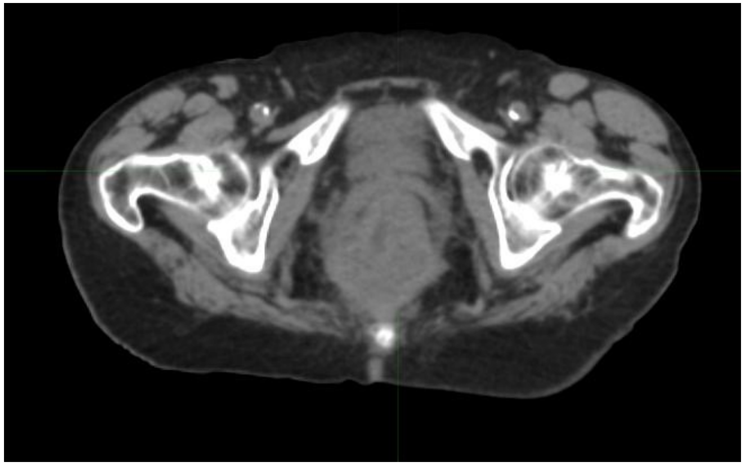


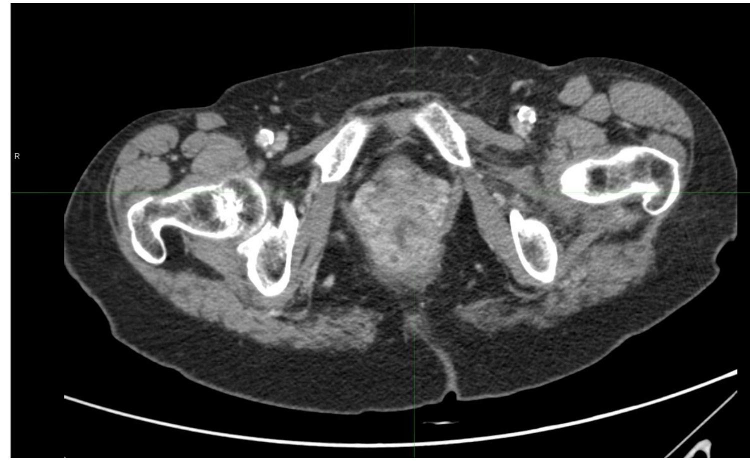
$$F_c = C_{sim} + \omega_{pen} C_{pen}$$

Regularization term: $1 + J_\tau J_\tau^{\,T}$; $1 + \det(J_\tau)$; K

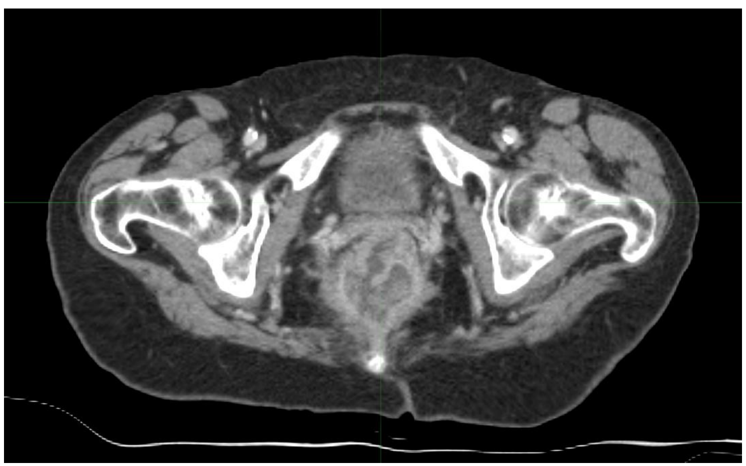
deformable registration - regularization



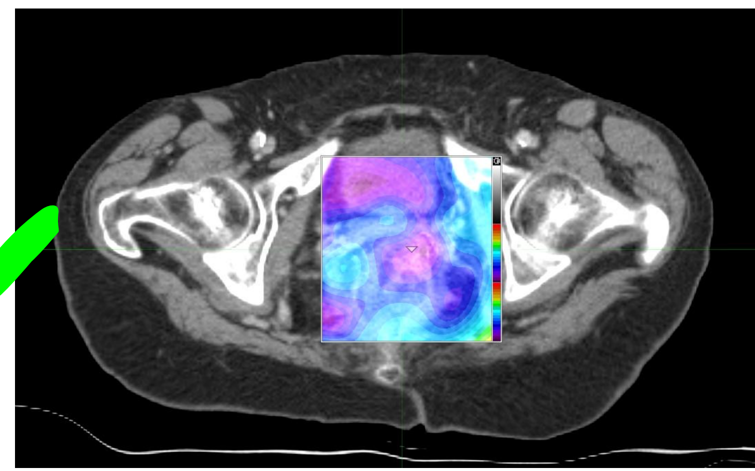
target



source



deformed



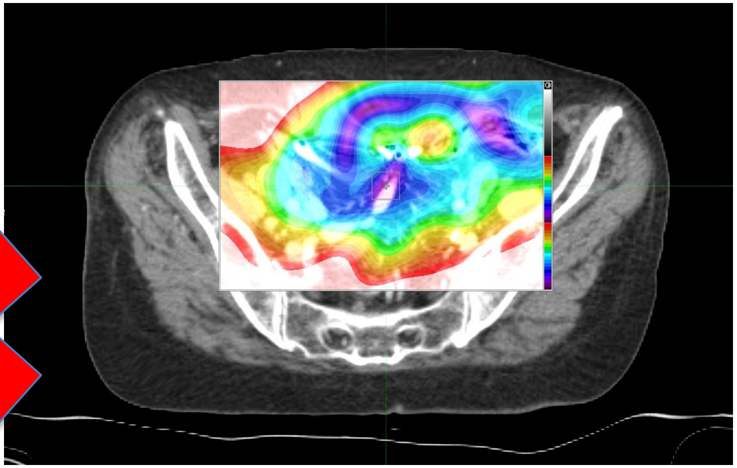
deformation map

deformable registration - regularization

target

source

deformed



deformation map

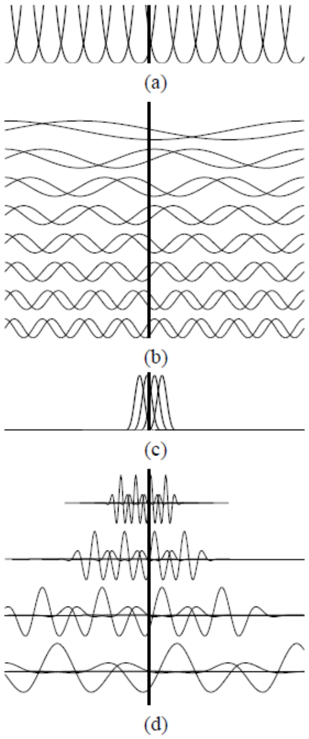
DEFORMABLE REGISTRATION - LUNG

-**B-spline-based** deformable registration

-continuous and differentiable functions

-simple implementation – calculation speed

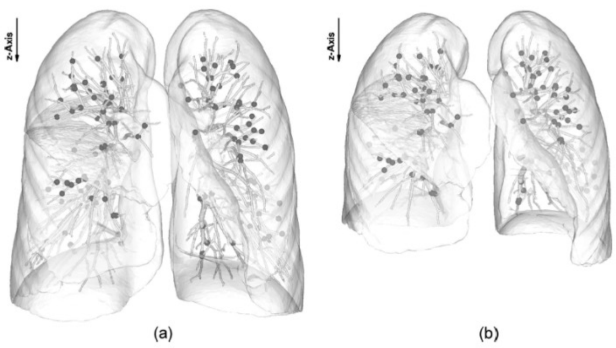
-critical aspects in “**anatomic discontinuities** “



DEFORMABLE REGISTRATION - LUNG

-**regularization**: conditions on the transf. Jacobian
-for example $D \cdot D^T = I$ or $J+1 = 0$ etc.

$$J(\mathbf{x};\phi) = \det(\mathbf{D}) \quad \text{with } \mathbf{D} = \begin{pmatrix} \frac{\partial T_x^c}{\partial x} & \frac{\partial T_x^c}{\partial y} & \frac{\partial T_x^c}{\partial z} \\ \frac{\partial T_y^c}{\partial x} & \frac{\partial T_y^c}{\partial y} & \frac{\partial T_y^c}{\partial z} \\ \frac{\partial T_z^c}{\partial x} & \frac{\partial T_z^c}{\partial y} & \frac{\partial T_z^c}{\partial z} \end{pmatrix}.$$

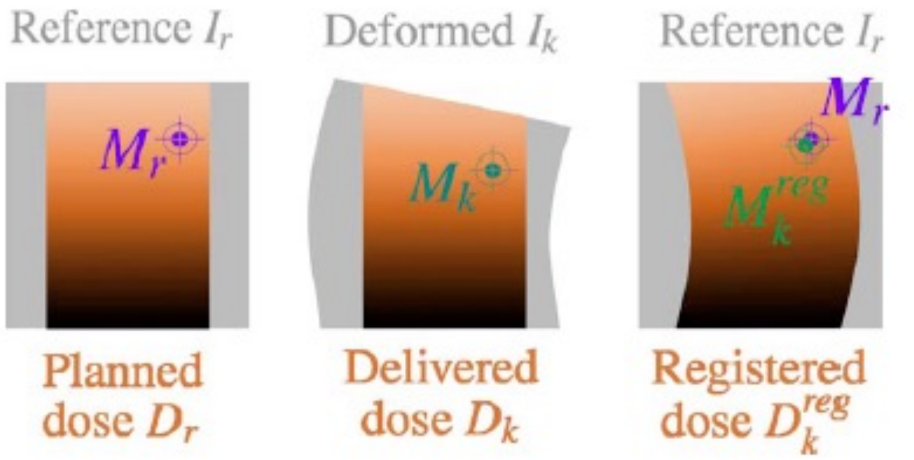


-corresponds to **volume preservation**
-**false** in general in the lung =>
alternative condition **mass preservation**

Y Yin, EA Hoffman, CL Linb, "Mass preserving nonrigid registration of CT lung images using cubic B-spline". Med. Phys. 36(9), 4213-4222 (2009).

IMAGE REGISTRATION – beyond multimodality image integration for treatment planning

-Dose tracking – dose accumulation in **Adaptive Radiation Therapy**



G Janssens, J Orban de Xivry, S Fekkes, A Dekker, B Macq, P Lambin, W van Elmpt, "Evaluation of nonrigid registration models for interfraction dose accumulation in radiotherapy". Med. Phys. 36(9), 4268-4276 (2009)

TAKE HOME MESSAGES

1. Image registration is the process that makes two or more image sets **spatially coherent to each other**

2. Applications to Radiation Oncology include **treatment planning and treatment verification/adaptation**

3. Rigid transformation is to be preferred, **if possible,** but deformations shall be considered as potential sources of error

4. Deformable registration is powerful (sometimes necessary) but difficult to control – expert judgment needed!

5. … see following module for other considerations on image registration applied to motion management …