Multimodal imaging

Enlight Meeting
Utrecht 2016

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Thanks to:

- Uulke van der Heide (Amsterdam NKI)
- Daniela Thorwarth (University Tübingen)
- Renata Raidou (Technical University of Eindhoven)
- Jesper Kallehauge (Aarhus University Hospital)
Multimodal imaging

Morphological imaging:
- Where is the tumour?
- What are the tumour characteristics?

Functional imaging:
- Where is the tumour?
- What are the tumour characteristics?

T2W MRI

DWI

CT

DCE-CT/MRI
Functional imaging modalities

- **PET**
  - Tracers accumulation reflect biologic processes as e.g. metabolism
  - Kinetics

- **MRI**
  - Spin relaxation depends on tissue structure
  - Contrast agents: kinetics

- **CT**
  - Contrast agents: kinetics
DCE-MRI
DCE-MRI

Semi-quantitative analysis
- Relative Signal Increase
- Area Under Curve

Quantitative analysis
- Extended Toft model ($K_{\text{trans}}$, $k_{\text{ep}}$, $v_p$)
  implemented as Murase et al.

\[
RSI(t) = \frac{SI(t) - SI(0)}{SI(0)}
\]

\[
AUC(t) = \int_0^t RSI(t) \, dt
\]

\[
C_t(t) = K_{\text{trans}} e^{-k_{\text{ep}}} \otimes C_p(t) + v_p C_p(t)
\]

Zahra et al. 2007
Hierarchy of models

2CXM
\((F_p, v_p, PS, v_e)\)

(Uptake regime)  \(PS/v_e \approx 0\)
\(F_p = \infty\)  (highly perfused)

C-TU
\((F_p, v_p, PS)\)

(intravascular regime)  \(PS = 0\)

1-CM
\((F_p, v_p)\)

ETM
\((K_{\text{trans}}, v_p, v_e)\)

\(v_p = 0\)  (weakly vascularized)

TM
\((K_{\text{trans}}, v_e)\)
Fitting of models

Fit comparison:

\[ AICC_m = n \cdot \ln \left( \frac{SS_m}{K_m} \right) + 2K_m + \frac{2K_m(K_m + 1)}{n - K_m - 1} \]

\( K_m \): # fit parameters
(TM=2, ETM=3, C-TU=3, 2CXM=4)
Diffusion weighted MRI (DWI)

- Measurement of diffusion of water molecules
- DWI is a quantitative method

Acquired data

Free diffusion

Restricted diffusion

\[ b = 200 \]

\[ b = 700 \]

\[ b = 1000 \]

\[ b = 1500 \]

\[ b = 2000 \]

**b-value:** changes the sensitivity of the diffusion length

\[ b = \gamma^2 G^2 \delta^2 (\Delta - \delta/3) \]

Provided by Jesper F. Kallehauge, Dept of Med Phys, AUH
Spatial resolution of functional imaging is challenging

Microscopy

Immunohistochemistry
(vascularization, perfusion, hypoxia)

Imaging

Clinical FMISO PET image, 4h pi

Courtesy E. Troost, Nijmegen
Image resolution

FMISO PET simulation 4 h pi
Functional Imaging with MRI and PET

Cell density, microanatomy
- DWI, DTI, $^{[18F]}$FDG

Perfusion, permeability of microvasculature
- DSC-MRI, DCE-MRI, $^{[18F]}$Galacto RGD, $^{[15O]}$H$_2$O

Cell membrane synthesis
- MRSI (choline), $^{[11C]}$Choline, $^{[18F]}$Choline

Metabolism
- $^{31P}$-MRSI, $^{[18F]}$FDG

Hypoxia
- R2* (BOLD), MRSI (lactate), $^{[18F]}$FMISO, $^{[18F]}$FAZA, $^{[18F]}$HX4
Combined PET/MR for Radiation Oncology

Visualization of anatomical, functional and molecular information of tumor tissue

Improved accuracy of target volume delineation based on PET/MR

Multi-parametric functional PET/MR imaging for biologically adapted RT dose prescriptions

\[ ^{68}\text{Ga}]\text{DOTATOC} \text{ PET/MR} \\
Boss A et al. JNM 2010; 51: 1198-205.
Combined PET/MR: Technical Realization

1. **Separate PET- and MR-systems**
   - Imaging systems in different rooms
   - Patient couch on rails
   - Time delay between PET- and MR image acquisition

2. **Co-planar PET/MR systems**
   - PET and MR back to back
   - Rotating table platform
   - 3T MRI plus TOF PET

3. **Integrated PET/MR**
   - MR-compatible PET detector ring inside clinical 3T-MR scanner
Integrated PET/MR: Technical Realization

- Simultaneous PET and MR acquisition

MR specification:
- 3T static magnetic field
- 60 cm bore size
- Spatial resolution < 1-3 mm

PET detector:
- MR-compatible PET components (APDs instead of PMTs)
- No time-of-flight (TOF) PET possible
Timing and purpose of imaging

● **Pre-treatment imaging:**
  - Location and characterisation of tumour
  - Target delineation
  - Differential dose prescription (e.g. dose painting)

● **Imaging during radiotherapy:**
  - Response monitoring
  - Adaptation of target volumes and treatment
  - Differential boosting
Pre-RT imaging and dose painting

Dose escalation in a functional PTV (f-PTV) vs. Hypoxia-guided Dose Painting by Numbers (DPBN) in Head and Neck Cancer.

(a) 54/60/70 Gy, standard IMRT

(b) 54/60/70/77 Gy, FDG-guided IMRT, f-PTV

(c) 54/60/70/84 Gy, FMISO-guided IMRT, DPBN

Thorwarth et al. IJROBP 2007
Imaging during radiotherapy

- Adaptation based on response
  - Imaging (or clinical assessment) during radiotherapy
  - Decision on treatment for residual target volume
  - Focal boosting with brachytherapy

- ICRU89: introduction of adaptive target concept (for CTV and GTV)
Radiomics

- Radiomics extracts a high number of features based on e.g. contrast, shape, texture, gradients etc.
- Patterns predicting disease failure are obtained with use of statistical modelling
Advanced tools for visualisation of multimodal imaging

e.g. Gleason Scores (GS)
Identification and Exploration of Intra-tumor Regions

t-Distributed Stochastic Neighborhood Embedding (tSNE) - L. van der Maaten, 2008
Anatomical space – feature space – cluster analysis
Why multimodality imaging in cervix cancer?

- Significant response during radiotherapy
  - Repeated imaging during radiotherapy
  - Individualised boosting with brachytherapy

- Hypoxia has significant impact on clinical outcome
  - Hypoxia imaging: DCE-MRI, FAZA, FMISO
Pre-RT 0Gy

DWI, b1000

T2W

Mid-RT 20Gy

Pre-BT 40Gy

ADC

0.72 ± 0.08

0.94 ± 0.12

1.11 ± 0.16
FDG PET

- Persistent PET to identify non-responders

Rationale: Link between imaging and biology

**Imaging and biology**

**Genetic profile**

**DCE MRI**

**Cancer Research**

*Hypoxia-induced gene expression in chemoradioresistant cervical cancer revealed by dynamic contrast enhanced MRI*

Cathinka Halle, Erlend Andersen, Malin Lando, et al.

*Cancer Res Published OnlineFirst August 13, 2012.*
DCE-MRI (RSI)
Mayr, Ohio

Pre-low - then high

Persistent low

(A) Local Tumor Control

(B) Disease-specific Survival

(C) Overall Survival

Mayr IJROBP 2010
18F-FAZA PET

- 15 pts repeated imaging:
  - pre-EBRT + after 30-40Gy

Schuetz et al, Acta Oncologica 2010
Currently, the majority of prostate cancer patients, the entire gland is treated:
- Surgery
- EBRT whole gland irradiation
- Brachytherapy LDR and HDR

Focal treatment upcoming:
- Multiple modalities: Radiotherapy: integrated boost or focal only, HIFU, Cryotherapy,...
- Question: how to delineate GTV?
How well can we delineate prostate tumors?

- 20 patients received mp-MRI prior to prostatectomy
- Tumors were delineated by 6 teams of a radiation oncologist and a radiologist
- Uncertainty about boundaries of tumors
- Difficult to detect small tumors (<0.5 cc)

From qualitative to quantitative imaging

- T2w \(\rightarrow\) T2 map
- T1w \(\rightarrow\) T1 map
- DWI \(\rightarrow\) ADC
- DCE-MRI \(\rightarrow\) \(K_{\text{trans}}\)
Validation of tumor probability model

<table>
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<tr>
<th>T2w</th>
<th>ADC</th>
<th>K$_{\text{trans}}$</th>
<th>H&amp;E</th>
<th>tumor probability</th>
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Calibration of tumor probability in 100 voxels that each have a probability of tumor presence of 50%, the histology should show that 50% of those voxels contain tumor and 50% do not.

Tumor probability and inter-observer variation

- The tumor probability correlates with the number of observers identifying a voxel as cancer

- Tumor probability model applied to the patients in the delineation study

Where should the field move?

- Novel image sequences and PET tracers
- Novel methods of image analysis
- Validation of link between imaging and biology
- Validation of link between imaging and outcome
- Exploitation of imaging for individualised, personalised, and adaptive radiotherapy