Radiation treatment planning in lung cancer

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1. The State-of-the-art in Radiation Oncology

versus
Current practice in Radiation Oncology

- Primarily based on snapshot CT prior treatment planning
- Motion taken into account by safety margins
- Treatment outcome (tumor and organs at risk) is correlated with dose distribution based on pre-treatment imaging

Target and organ at risk segmentation is a key step in the treatment chain
Margins and Image Guidance

Geometric uncertainties are commonly accounted for by margins
Target volume concepts in Radiation Oncology

- The International Commission on Radiation Units and Measurements (ICRU) has as its principal objective the development of internationally acceptable recommendations
  - Quantities and units of radiation and radioactivity
  - Procedures suitable for the measurement and application of these quantities in clinical radiation oncology and radiobiology

ICRU defines a common language for clinical practice in Rad Oncol
ICRU volume concepts

- ICRU concepts were traditionally based on morphology/anatomy
- Margins account for temporal effects
- Concepts are in transition...

Target concepts imply structure boundaries!
Current Imaging Standards in RO

- CT with flat table top plus room laser
- MRI mainly for brain lesions
- Image Guided beam delivery
- PET/CT not for every patient

CT is the imaging workhorse in radiation oncology

CT number = 1000 \left( \frac{\mu_i - \mu_w}{\mu_w} \right)
Intensity Modulated Radiotherapy (IMRT)

- Inversely planned IMRT allows dose “sculpting”
- High degree of dose conformity implies risk of geographic misses if target definition is not at highest level of accuracy

IMRT enabled a new level of dose conformity
Today’s Technology for Image Guidance

- Beam quality
  - MV (3 – 6 MV)
  - kV (80 – 130 kV)

- Beam collimation
  - CBCT
  - FBCT

- Dimensions
  - 2D
  - 3D

- Rail-track-, ceiling/floor-, gantry-mounted

Current IGRT technology on/in the linac is X-ray based
2. Limitations in practice & ways to improve

“The difference between theory and practice ...”

... is larger in practice than in theory !”

John Wilkes
Inter- & intra-observer variations

**Steenbakkers et al R&O (2005)**
- 11 radiation oncologists (5 institutions) delineated 22 lung targets

**Hurkmans et al IJROPB (2001)**
- 4 radiation oncologists, each 3 times following a protocol – 1 patient
- Same institution

**Rasch et al RO (2010)**
- 10 radiation oncologists delineated 10 pts

Multimodality imaging and education reduce inter-observer variations
FDG based PET for target delineation

- “Proven” for NSCLC
  - Evidence for head-and-neck, lymphomas, esophageal cancer
- Most important applications for Radiation Oncology
  - Lymph node staging
  - Lung: differentiation of atelectasis and tumor tissue

In curative treatments the target should be small and accurate

Mac Namus et al R&O 91 (2009)
- Sensitivity: PET 83%, CT-64%
- Specificity: PET 91%, CT-74%
Gambhir 2001
- 16 Studies, 1355 patients
FDG based PET for target delineation - NSCLC

• Improved consistency: YES
• Closer to ground truth: unproven.....

PET-CT based target definition has become standard in many departments

Steenbackers et al IJROBP 2006

CT
St. dev. 1.0 cm

PET-CT
St. dev. 0.4 cm
**Important reading**


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Radiotherapy and Oncology

IAEA consensus report

**PET/CT imaging for target volume delineation in curative intent radiotherapy of non-small cell lung cancer: IAEA consensus report 2014**

Tom Konert\(^{a,b,*}\), Wouter Vogel\(^{a,b}\), Michael P. MacManus\(^{c}\), Ursula Nestle\(^{d}\), José Belderbos\(^{b}\), Vincent Grégoire\(^{e}\), Daniela Thorwarth\(^{f}\), Elena Fidarova\(^{g}\), Diana Paez\(^{h}\), Arturo Chiti\(^{i}\), Gerard G. Hanna\(^{j}\)

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**ABSTRACT**

This document describes best practice and evidence-based recommendations for the use of FDG-PET/CT for the purposes of radiation therapy target volume delineation (TVD) for curative intent treatment of non-small cell lung cancer (NSCLC). These recommendations have been written by an expert advisory group, convened by the International Atomic Energy Agency (IAEA) to facilitate a Coordinated Research Project (CRP) aiming to improve the applications of PET based radiation treatment planning (RTP) in low and middle income countries. These guidelines can be applied in routine clinical practice of radiotherapy TVD, for NSCLC patients treated with concurrent chemoradiation or radiotherapy alone, where FDG is used, and where a calibrated PET camera system equipped for RTP patient positioning is available. Recommendations are provided for PET and CT image visualization and interpretation, and for tumor delineation using planning CT with and without breathing motion compensation.

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3. Exploration of PET-CT in Radiation Oncology

Totally \textit{DOABLE}

EXPLORATION WAY
**Outcome monitoring**

*Latifi et al* “Study of 201 non-small cell lung cancer patients given stereotactic ablative radiation therapy shows local control dependence on dose calculation algorithm” *IJROBP* 2014;88:1108-13

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**Fig. 1.** Cumulative incidence of recurrence by group for all patients (N=201): pencil beam (PB) versus collapsed cone convolution (CCC).

**Fig. 3.** Example of pencil beam (PB) algorithm dose overestimation compared with collapsed cone convolution (CCC) algorithm in a patient receiving 50 Gy in 5 fractions. Positron emission tomography recurrence image is overlaid with the planning computed tomographic image showing the planning target volume (PTV) and prescription isodose for both treatment planning systems. (A) PB treatment plan reflecting PTV D95 of 50 Gy. (B) CCC recalculation shows underdosage: PTV D95 = 43 Gy.

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Dose calculation algorithm has an impact on RT outcome
NSCLC response assessment with FDG

- 34 patients
- 2 year FU

“Measuring early response is feasible by measuring the decrease in average FDG uptake after 2 weeks of radiotherapy”

PET seems superior to CT for response assessment (in a research setting)
Perspectives for next decade(s)

• Biological optimization
  ➔ Tumor
  ➔ Tolerance doses to OAR are driving optimization in IMRT

• Intra-tumor heterogeneity
  ➔ Tissue characterization
  ➔ Multi-parametric imaging (CT, MR, PET)

• Inter-patient heterogeneity
  ➔ Imaging and intensified follow-up

“Biological” adaptations are new degrees of freedom in RO treatments
4. Technical issues
Adaptations of imaging systems for RO

- Imaging for treatment planning needs to be performed in treatment position
  - Flat table top, immobilization devices + indexing, laser (coordinate system with linac), correlation with dose, ....

- PET-CT can replace planning CT at radiotherapy

PET-CT for target definition should be directly used for treatment planning
“Quantitative” Imaging

- Tumor volume delineation in RO implies “boarders”
- PET-CT in lung implies motion challenges
- What protocol should be used (to exclude inter-observed variation)?
  - Visual vs. semi-automated vs. automated?
  - Absolute SUV (e.g. 2.5)
  - Relative (e.g. 40%, 50% of maximal intensity)
  - Contrast-dependent adaptive threshold (background)

Protocols are of outmost importance (Windowing, timing, ...)


Olsen et al. JMRI 37 (2013)

Scanner & image reconstruction aspects

- Multi-centric studies are upcoming in radiation oncology
  - Need for large patient cohort studies
- Quality assurance and standardization is a prerequisite
  - Many free parameters in PET image reconstruction have an impact

Collaboration of Radiation Oncology and Nuclear Medicine QA is required
Scanner & image reconstruction aspects

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Collaboration of Radiation Oncology and Nuclear Medicine QA is required
Summary

- Hybrid imaging has high potential to improve RO
  - Not limited to planning and target definition
  - Not limited to current indications and techniques
- Dose “thinking” in Radiation Oncology moved from 3D to 5D
  - geometry/morphology, temporal variations, tissue characteristics and response to therapy
  - “One size fits” all is outdated
- Implementation of quantitative imaging for RO requires multi-disciplinary efforts
Acknowledgements

Visit http://www.meduniwien.ac.at/hp/radonc/

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and many others ......
Technology evolution in Radiation Oncology

- **Conformity**
  - Stereotactic Radiotherapy
  - 3D
  - Volumetric Modulated RT
  - Cyberknife
  - Tomotherapy
  - Linac MR
  - Ion Beam Therapy
  - **Main difference via**
    1. Higher precision through better integration of imaging and
    2. More interfaces between „machines“, user, and between professions

- **Sophistication**
- **Continuous improvement in beam delivery & dose conformality**
Patient Specific QA Procedures

Patient specific QA procedures are often not patient related

Real  Virtual (Digital environment)

CT imaging

4D CT phases (1 cycle)

Dose calculation

Treatment planning

Delineation ROI

Pre-treatment QA

Pre-treatment imaging

Digital Patient Model

Phantom

Patient
Optimization of radiotherapy planning of patients with inoperable locally advanced non-small-cell lung cancer with FDG-PET
PI: U. Nestle, Department of Radiation Oncology, Univ. of Freiburg, Germany

Prospective randomized multicenter therapy optimizing trial
21 Centers, 396 Patients, Start: Nov. 2009

**Arm A:** CT based target volume delineation / **Arm B:** PET based target volume delineation
Dose escalation study. Dose limitation: tolerance of normal tissue
End point: Local tumor control
Lung cancer: Inter-observer-variation (IOV)

• Gambhir 2001
  ➔ Sensitivity: PET 83%, CT-64%
  ➔ Specificity: PET 91%, CT-74%
  ➔ 16 Studies, 1355 patients

Nestle et al R&O 2006

PET-CT based target definition changes has become standard in many RT departments
Outline

• SBRT specific requirements
• Characteristics of FFF photon beams
• Commissioning of linac and TPS  
  ➔ Dose calculation accuracy  
  ➔ Detector specific issues for FFF beams
• Treatment delivery options for SBRT
• Periodic QA  
  ➔ (Machine specific) – imaging systems  
  ➔ Patient specific QA
• Conclusions / Summary
SBRT features and resulting requirements

- High (fractional) doses
- Rather small targets imply small fields w/o intensity modulation
- Image Guidance “standard” to enable high geometric precision – robotic tables
- Heterogeneities often present
- Respiration management during imaging and treatment delivery

“advanced” C-arm linac is common workhorse for SBRT
Real time motion tracking – paired kV – MV sets

- Imaging dose: ~ 100 mGy per beam

Motion tracking for image guided beam delivery is feasible

Furtado et al Acta Oncol (2013)
Learning objectives

To understand
• Techniques and workflow in precision radiation therapy
• Uncertainties in target volume definition
• Technical requirements for imaging

Appraise
• Added value of PET based target definition
• Potential contribution of PET in response assessment