4D/IMRT/SBRT: Does Technology Improve Outcomes?

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UCSF RADIATION ONCOLOGY UPDATE:
CONTROVERSIAL ISSUES IN CONTEMPORARY PRACTICE

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I have received research support from Accuray, the maker of the CyberKnife system
Advancements in lung RT

1. Managing respiratory motion (4DCT, gating, real time tracking)

2. Treatment planning and delivery techniques that allow to tightly conform the dose to the target

3. Dose calculation algorithms that allow to accurately calculate the dose in low density lung tissue
Outline

- Does technology improve outcomes?
  - SBRT for early stage lung cancer
    - Tracking methods
    - Treatment planning
    - Dose calculation algorithms
  - IMRT for advanced stage lung cancer
    - Discuss potential benefits of IMRT
    - Review clinical studies
Dynamic Tracking

- At UCSF, we perform lung SBRT with CyberKnife
- A unique capability of CyberKnife is dynamic tracking
- Radiation delivery is synchronized with target motion in real time

- Patients breath normally
- 100% duty cycle
- Variations in target motion pattern are detected and accounted
- No need for ITV creation
Static Tracking

- Not all patients are candidate for dynamic tracking
- No implanted fiducial or tumor not visible in 2D images
- Bony landmarks in the spine are used for alignment
- About 60% of lung SBRT patients at UCSF

- No tumor motion tracking
- ITV needs to be generated
- Corrections are calculated at the spine. Large deviations might occur far away from the alignment center
Treatment planning

- Highly conformal dose to the target with steep dose gradient and sparing of adjacent critical structures
- Hundreds of non-isocentric/non-coplanar beams aimed at the target
Planning Study – Early stage

- Compared dose distribution and risk of radiation pneumonitis (RP) among 3 SBRT modalities: VMAT, Tomotherapy and CyberKnife
- 9 patients with central tumors \( \leq 5 \) cm
- Plans were developed per RTOG 0813 guidelines using same contours
- Target coverage and conformity were similar across modalities
- CK and VMAT plans resulted in lower risk of RP then Tomo plans

Kannarunimit et al, TCRT 2014, In press
Dose calculation algorithms

- Dose calculation must account for tissue heterogeneity
- Monte Carlo (MC) is the most accurate method for dose calculation
- Simple techniques employing equivalent path length corrections (RT) produce largely inaccurate results in the lung [1]
- We compared the dose distribution calculated by RT and MC and found that RT over-estimated the dose to the target by 10-30% [2]

Dose MC improve outcomes?

- Using MC we are effectively prescribing higher dose
- We compared the clinical outcomes of locoregional control (LRC), disease free survival (DFS), overall survival (OS) and toxicity as a function of the calculation method (RT vs. MC)
- Cohort of 31 early NSCLC patients
- Local control and long-term toxicity appear independent of the dose calculation method

Braunstein et al, J. Radiosurgery and SBRT (2014) In press
MC - Discussion

- Although no evidence of improved local control or survival emerged from this study – we strongly believe in the clinical implementation of Monte Carlo

- It is possible that improved LRC will be achieved through routine use of MC-based higher target dose

- The lack of impact of dose calculation method on disease control could be due to a significant tumor response over a wide range of BED

- Although target dose for MP plans was 10-30% higher, there was no evidence of increased toxicity

- Accurate dose calculation is pivotal in order to standardize outcomes analysis in multi-center trials
Technologies for advanced stage

- Dosimetric studies comparing 3D-CRT with IMRT have been reported for advanced stage lung cancer patients
- Multiple fields and intensity modulation
Techniques that reduce the normal lung dose should reduce the risk of radiation pneumonitis (RP)

- Compared to 3D-CRT, IMRT resulted in lower lung $V_{10}$ and $V_{20}$ and in lower dose to esophagus and heart
- IMRT resulted in higher lung $V_{5}$

- Compared to 3D-CRT, IMRT resulted in reduced dose to the lung
Potential issues of IMRT

- **Dose painting**: in IMRT the target is not always fully included in the radiation field
- The interplay between respiratory motion and dose painting creates the potential for dosimetric misses.
- Physics studies have demonstrated that these effects are likely to be compensated during the course of treatment [1-3]
- **Low level dose to lung**: increase of V5 might contribute to RP
- **Increase of integral dose** might cause radiation-induced cancers
- **Clinical studies investigating outcomes are needed**

Study from MD Anderson

Investigated the rate of Grade ≥3 treatment-related pneumonitis in patients treated with IMRT compared to 3D-CRT

IMRT resulted in significantly lower rate of pneumonitis compared to 3D-CRT (8% vs. 32% at 12 months)
Study from MD Anderson

Comparison of CT/3DCRT and 4DCT/IMRT on disease outcomes and toxicity in patients with unresectable, locally advanced NSCLC treated with concomitant chemotherapy
Study from MD Anderson

- Largest single-institution retrospective study
- CT/3DCRT $\rightarrow$ n=318; median dose 63 Gy (50-73 Gy)
- 4DCT/IMRT $\rightarrow$ n=91; median dose 63 Gy (50-72 Gy)
- Disease end points were locoregional progression (LRP), distant metastasis (DM) and overall survival (OS)
- Toxicity endpoint was radiation pneumonitis Grade $\geq$ 3
- Lung parameters: Mean dose, V5, V10 and V20
- The 4DCT/IMRT group had more favorable OS and lower RP
- Reduction in toxicity seems due to an improved lung dose

Liao et al, IJROBP 76(3) 775, 2010
Study from Stanford

A Population-Based Comparative Effectiveness Study of Radiation Therapy Techniques in Stage III Non-Small Cell Lung Cancer

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- SERR-Medicare database to compare effectiveness of IMRT, 3D-CTR and 2D-RT in stage III NSCLC
- 3D-CRT and IMRT had superior outcomes compared to 2D
- IMRT was associated with similar survival and toxicity risk compared to 3D-CRT
In early stage patients:

1. SBRT has been increasingly employed with favorable outcomes
2. Dynamic tracking improved clinical outcomes
3. Advanced modalities can reduce the lung dose and the risk of radiation pneumonitis
4. Importance of using Monte Carlo

In advanced stage patients:

1. IMRT produces a more conformal dose distribution with lower dose to lung and other critical structures
2. IMRT was associated with lower lung toxicity and improved survival
Conclusions

- Does technology improve outcomes?
- Definitively technology improves *physics outcomes*
- Thanks to technological advancements we are now able to control the dose distribution, to precisely deliver dose to a moving target, and to verify the treatment accuracy
- If physics outcomes do not translate into clinical outcomes, it means that we are not looking at the right parameters (i.e. V20?)
- Now that we have the right technology, the next step is to work with the clinicians to define the clinically relevant parameters
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