Heterogeneity Corrections in Clinical Trials

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Lung Trials: Effect of Low Density Tissue

Need for accurate dose algorithms

- Effectiveness of radiation therapy depends on maximum TCP and minimum NTCP. Both of these quantities are very sensitive to absorbed dose
- We learn how to prescribe from clinical trials and controlled studies. Their outcome depends on the accuracy of reporting data

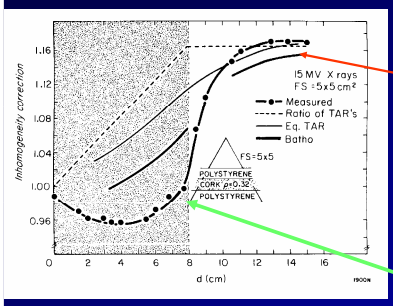
Inhomogeneity Corrections Clinical Examples

- Mah & Van Dyk (1991)
  - reviewed 100 thoracic patients
- Conclusions
  - Within lung, corrections are significant (0.95-1.24)
  - Target dose corrections are significant (0.95-1.21)
  - Substantial variation over patients (-5% to +21%)
  - Dose uniformity reduced in corrected distributions
  - In ~80% patients, probability of lung damage underestimated by >5% (up to 19%) if corrections not applied

Inhomogeneity Corrections Clinical Examples

- Orton *et al (1998)*
  - Developed benchmark test case
  - Reviewed 322 patients enrolled in RTOG 88-08
- Results
  - Benchmark lung corrections
    - Measured: 1.14 (Co-60)-1.05 (24 MV)
    - Calculated: 1.17 (Co-60)-1.05 (24 MV)
  - Patients: 0.95-1.28, mean=1.05, SD=0.05
    - For lateral fields: mean=1.11, SD=0.08
- Conclusion
  - Lung corrections lead to significant variations
  - Density corrections will help reduce these variations

Why you could correct in wrong direction..



Relying on data within the tumor will lead you to reduce MU

But at the interface there is an underdose

In summary: MU will likely not change, so neither will prescriptions

Lung Corrections - Controversies

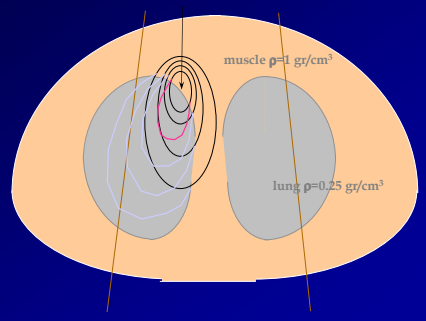
- **Ekstrand *et al* (1990) Pitfalls in the Use of High Energy X Rays to Treat Tumors in the Lung**
  - **measured penumbra in low density**
  - **electron transport corrections are needed**
  - **in the mean time, use 6 MV x-rays**
- **Klein *et al* (1997) A Volumetric Study of Measurements and Calculations of Lung Density Corrections for 6 & 18MV Photons. (RTOG 9311 era)**
  - **"The deficient coverage of PTV2 by the 18 MV beam compares unfavorably with the slight increase (5%) in hot spots associated with 6 MV. Our studies support strong caution before reducing dose prescriptions based on simple algorithms."**

RADIATION THERAPY ONCOLOGY GROUP
RTOG 0412/SWOG S0332

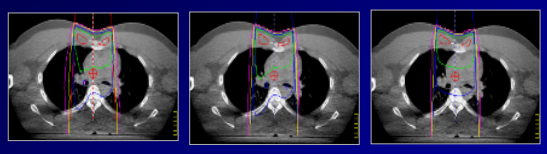
PHASE III RANDOMIZED TRIAL: STAGE IIIA (N2) NON-SMALL CELL LUNG CANCER

6.4.1 *Dose Calculation*: Doses are to be calculated **with heterogeneity correction**, i.e., correction is to be made for density differences between air spaces, lung, water-density or bony tissue. Treatment planning should be performed in accordance with the prescribing doses to each target, together with restrictions in dose to normal tissues…….

Convolution/Superposition: Heterogeneities

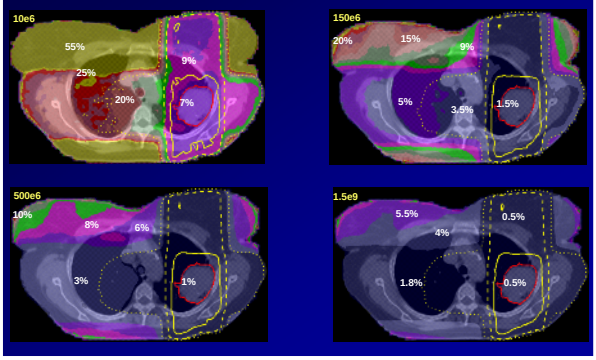


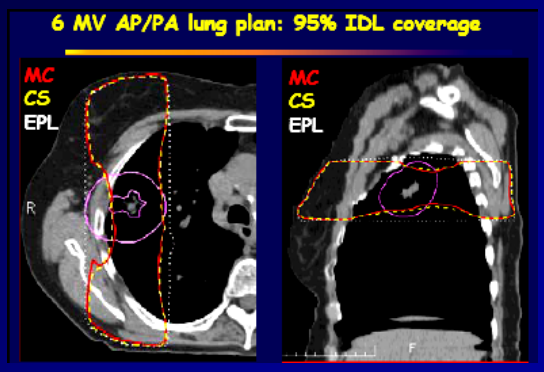
Convolution Lung Calculation



Convolution/Superposition | Homogeneous Scatter | Homogeneous Primary and Scatter

Monte Carlo Calculations:
Dependence on Statistics (# Histories)





Chetty, AAPM 2006

TG-65: Published in August of 2004

TISSUE INHOMOGENEITY CORRECTIONS FOR MEGAVOLTAGE PHOTON BEAMS
Report of Task Group 65 of the Radiation Therapy Committee of the American Association of Physicists in Medicine

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TG-65 Recommendations

- **The physicist should understand the dose calculation resolution grid, due to volumetric averaging.**
- **The physicist should maintain an open dialogue with clinicians and be clear on limitations of the TPS. For each clinical site (eg. left breast, right lung, larynx etc), there should be 5-10 treatment plans generated, with & without inhomogeneity corrections. The dose prescription should be the same for both cases.**

TG-65 recommends energies of 12 MV or less for lung radiotherapy.

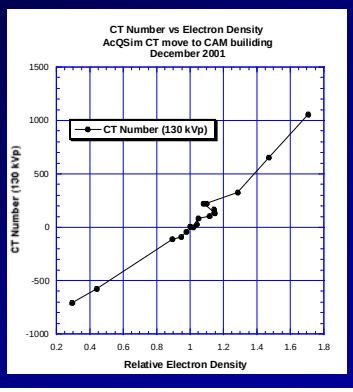
Current Practice: Prescription

- **Heterogeneous plan used for *up-front* MU**
- **Great care is taken to have weight points in tissue media (even of not isocenter)**
- **Dose prescribed to 95% isodose**
- **i.e., 7095cGy @ 95%, 7468cGy @ Isocenter**

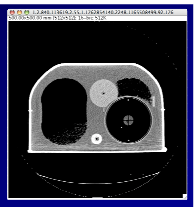
Limited to 6 MV 3mm Resolution

Our Resultant MU nearly the same as water-based calculations

CT number to electron density



RPC: Credentialing for Lung Protocols



- RPC evaluates dose to TLDs
  - Criteria: ± 0.05
- Evaluate DTA from film data
  - ± 5 mm at all sides of target
- Analysis neglects variation across target
  - RPC has proposed to include evaluation of dose across target

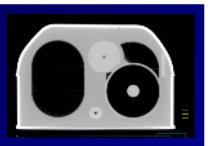
TLD Dose vs. Hetero Corrected Plan

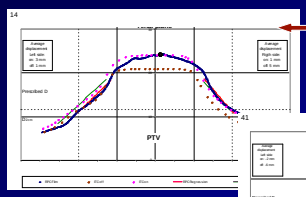
TPS	Dose Calc. Algor correction on	Number of irradiations	D_{TLD}/D_{hetero}
Precise v 2.01	Scatter Integ. Clarkson Type	2	0.99 ± 3.1%
BrainLab	Clarkson & Pencil Beam	4	0.96 ± 2.7%
Eclipse	Pencil Beam	2	0.97 ± 1.6%
Ergo	3D Convolution Pencil Beam	1	0.98 ± 3.2%
Pinnacle v 6.2, 6.4, 7.0g, 7.4f	Adaptative Convolve	8	0.99 ± 2.3%
Render plan	Change in primary attenuation	1	0.92
XiO	Superposition/Convolution	3	0.96*
	Total	21	0.97

Summary of Systems Passing Existing Criteria

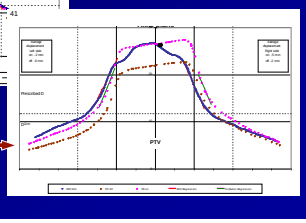
System/Algorithm	Percent of Points Within: 5%	7%	10%
Pencil Beam-Clarkson	69 ±28%	82 ±14%	91 ±8%
Convolution-Superposition	88 ±23%	96 ±13%	98 ±7%

Evaluation of Heterogeneity Corrections with RPC Thorax Phantom





Convolution/superposition algorithm showing good agreement with measurements



Pencil-beam algorithm showing poor agreement with measurements

Conclusion

- The Radiotherapy Community has finally put everything together……
  - Robust Algorithms
    - Superposition/Convolution
    - AAA
    - MC, etc.
  - Credentialing – the RPC
  - Methods to Test and Transition to Using Up-Front Corrections
- …to Properly Run Clinical Trials for Thorax Irradiation (incl. SRS)