UNIVERSITY OF WISCONSIN
SCHOOL OF MEDICINE
AND PUBLIC HEALTH

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Future Monte Carlo Applications in Medicine

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Future Monte Carlo applications

- **Past:**
  - MC-based radiation dosimetry – had a profound effect on dosimetry standards **(Rogers)**
  - MC-based treatment planning – most likely will become a standard in the future **(Kawrakow, Rogers)**
  - MC proton and heavy ion simulations – more and more widespread **(Jones, Qaim, Paganetti, Wambersi)**
- **Present and Future:**
  - MC-based intensity modulated radiotherapy (IMRT)
  - MC-based image-guided radiotherapy (IGRT)
  - Continuous MC simulations (spatial and temporal)
  - MC-based adaptive radiotherapy
  - MC-based non-transport applications

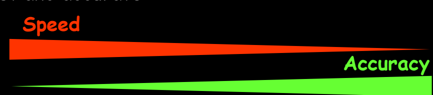
Monte Carlo-based Intensity Modulated Radiation Therapy

Intensity modulated radiation therapy

- All commercial IMRT systems use non-Monte Carlo-based dose calculations (pencil beam or convolution/superposition)
- Questions:
  - Is inclusion of Monte Carlo calculated dose into inverse treatment planning trivial?
  - How does MC-based IMRT compare to the non-MC-based IMRT?
  - Can we speed up Monte Carlo-based IMRT?

Correction vs model-based dose calculation

- Dose calculation for treatment planning has to be fast and accurate



Correction-based — **Model-based**

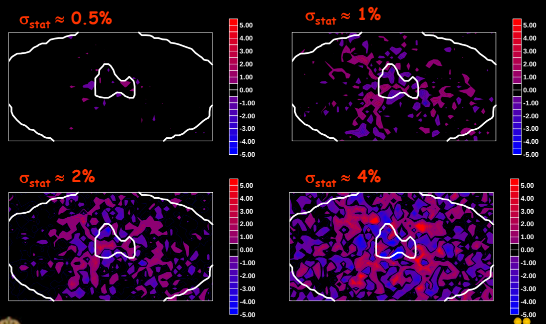
Pencil beam — C/S — Monte Carlo

- Inverse treatment planning for IMRT requires calculation of multiple dose beamlets many times…
- Is Monte Carlo dose calculation feasible at all?

Monte Carlo-based IMRT

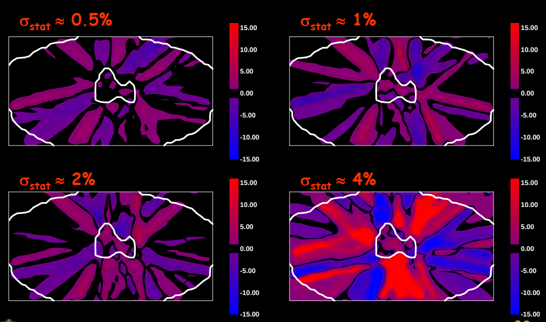
- If Monte Carlo-based dose calculation is used we face two errors:
  - **Statistical error** because of the statistical noise itself
  - **Noise convergence error** because optimisation converges to the optimal solution for the noisy beamlets, which is not optimal for the noise-free beamlets

Statistical error



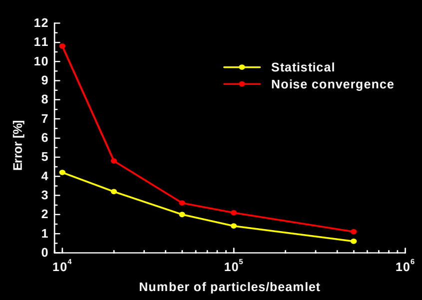
Jeraj and Keall, Phys Med Biol 45, 2000, 3601

Noise convergence error



Jeraj and Keall, Phys Med Biol 45, 2000, 3601

Dependence of errors

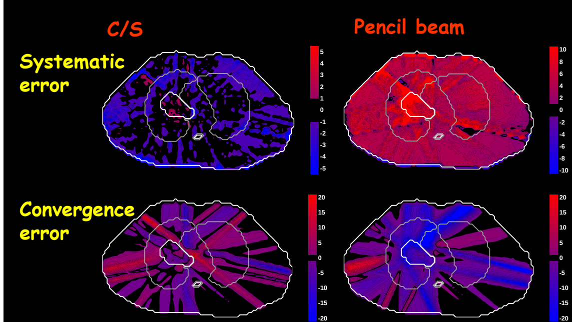


Jeraj and Keall, Phys Med Biol 45, 2000, 3601

Non-Monte Carlo-based IMRT

- If non-Monte Carlo-based dose calculation is used we face two errors:
  - **Systematic error** because of the inaccurate dose calculation
  - **Convergence error** because optimisation converges to the optimal solution for the inaccurate beamlets, which is not optimal for the accurate beamlets

Errors



Jeraj *et al*, Phys Med Biol 47, 2002, 391

Errors for lung case

C/S dose calculation

Error [% D_{max}]	Tumour	Lung
Systematic	-0.1 ± 2	-1 ± 1
Convergence	$0.1\text{-}0.8 \pm 2\text{-}5$	$0.5\text{-}1 \pm 1\text{-}4$

Pencil beam dose calculation

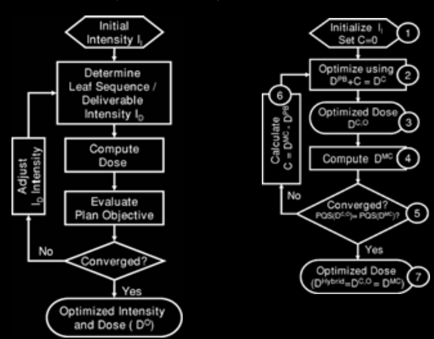
Error [% D_{max}]	Tumour	Lung
Systematic	$+8 \pm 3$	$+6 \pm 5$
Convergence	$7\text{-}10 \pm 3\text{-}5$	$7\text{-}8 \pm 6\text{-}7$

Jeraj *et al*, Phys Med Biol 47, 2002, 391

When is Monte Carlo dose calculation of advantage?

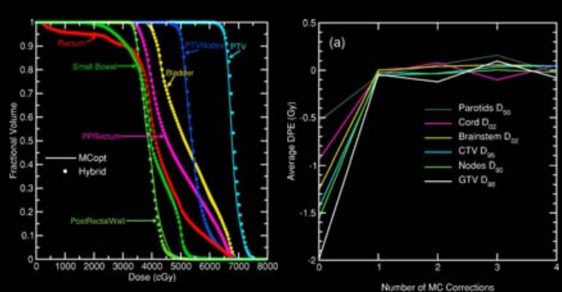
- Monte Carlo dose calculation can be of advantage in IMRT only if the statistical error is <2%
- If the statistical error is >2% than the statistical errors and noise convergence errors are higher/comparable to systematic errors and convergence errors of the plans calculated with C/S dose calculation
- Note that Monte Carlo dose calculation includes some fraction of the systematic error due to inaccurate commissioning

Hybrid optimization



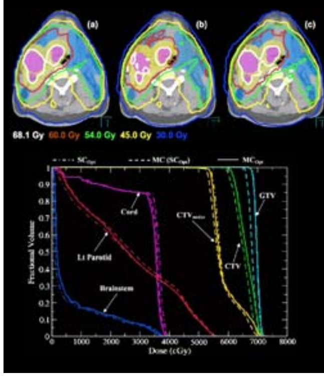
Siebers *et al*, Med Phys 34(7), 2007, 2853

Fast convergence – no compromise in accuracy



Siebers *et al*, Med Phys 34(7), 2007, 2853

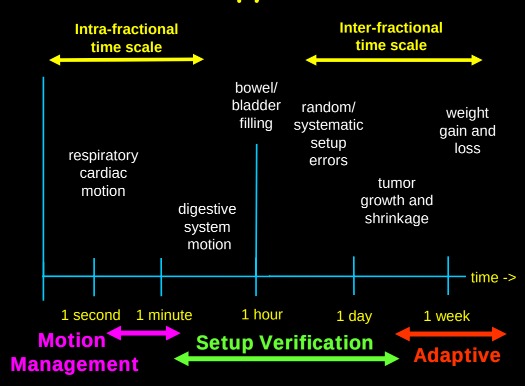
Summary: MC-based IMRT



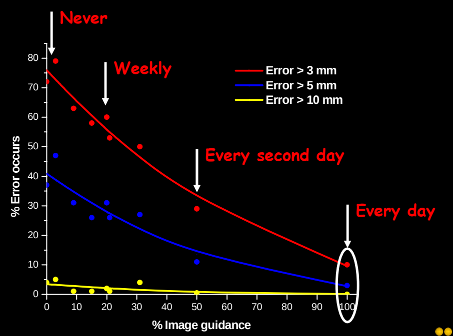
- Clinically significant in heterogeneous regions (e.g., head and neck, lung)
- Not clinically significant in homogeneous regions (e.g., prostate)
- If you have it, why not use it
- Underlying uncertainties due to inaccurately known source
- Noise

Monte Carlo-based Image-guided Radiation Therapy

Radiotherapy time-scales



Residual errors for image-guidance

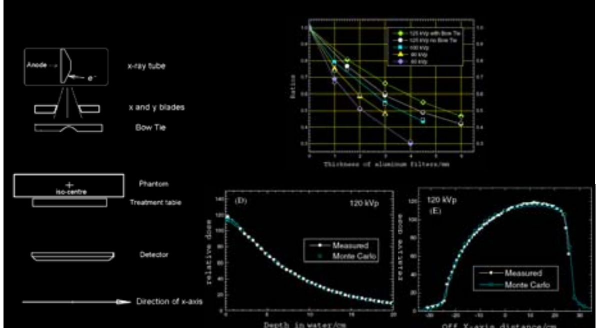


Zeidan *et al*, Int J Rad Oncol Biol Phys 67, 2007, 670

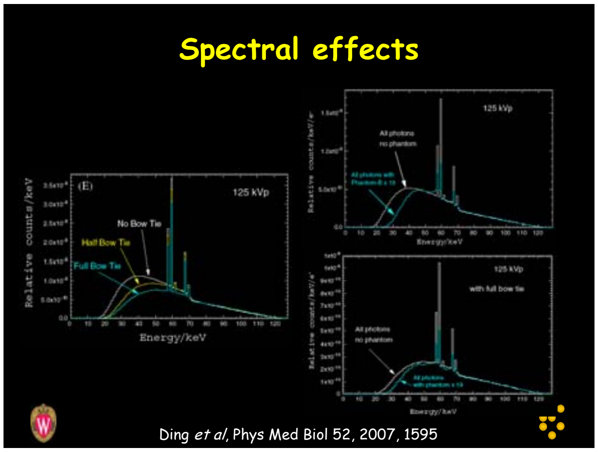
Image-guided radiation therapy

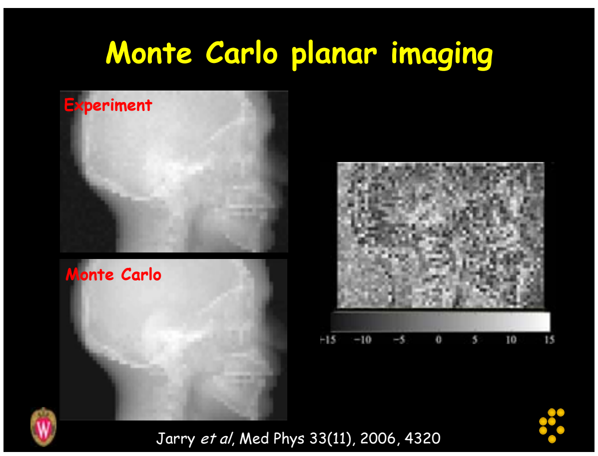
- Image-guidance can clearly improve the accuracy of therapy, the question is whether Monte Carlo has anything to add there
- Questions:
  - Can Monte Carlo simulations be used for optimization of imaging systems
  - Can Monte Carlo simulations be useful for characterization of kV and MV imaging sources
  - Can Monte Carlo simulations help with the imaging scatter

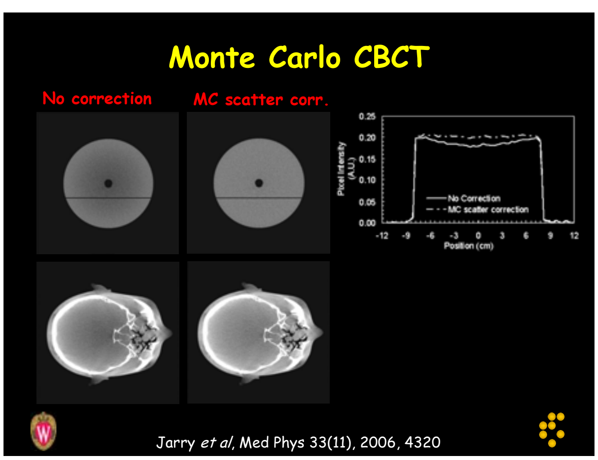
Simulations of a kV CBCT source



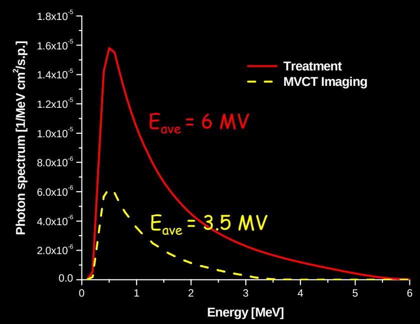
Ding *et al*, Phys Med Biol 52, 2007, 1595


Spectral effects
125 kVp
No Bow Tie
Half Bow Tie
Full Bow Tie
Relative counts/keV
Energy/keV
All photons no phantom
with full bow tie
Ding et al, Phys Med Biol 52, 2007, 1595

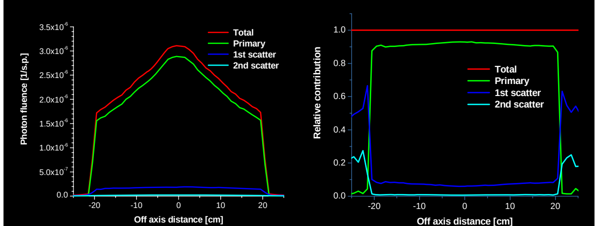

Monte Carlo planar imaging
Experiment
Monte Carlo
−15 −10 −5 0 5 10 15
Jarry et al, Med Phys 33(11), 2006, 4320


Monte Carlo CBCT
No correction
MC scatter corr.
Pixel intensity (A.U.)
No Correction
MC scatter correction
Position (cm)
Jarry et al, Med Phys 33(11), 2006, 4320

MV imaging on helical tomotherapy

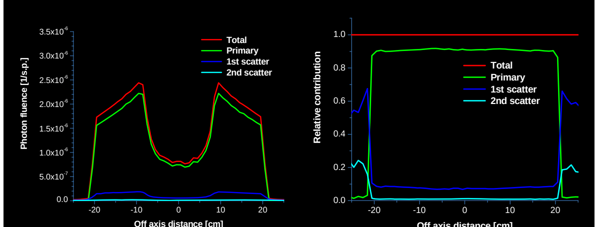


Helical tomotherapy
no patient



No object in the beam - only 10% of scattered photons **- very clean beam**

Helical tomotherapy
head and neck patient



Patient in the beam – scatter does not increase significantly **– excellent for imaging**

Summary: MC-based IGRT

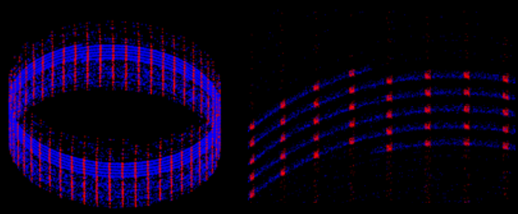
- Monte Carlo simulations of imaging systems can reveal many useful details that can be used in their characterization and optimization
- Particular important application is estimation of the scatter, which can be used to improve the imaging quality

Continuous Monte Carlo Simulations

Continuous therapy – continuous simulations

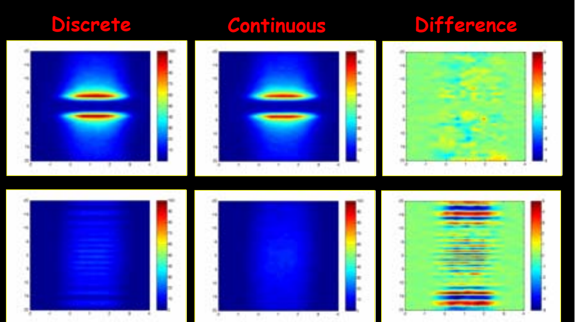
- Radiotherapy treatment is a dynamic process:
  - Source motion
  - Collimator motion (MLC)
  - Patient motion
- Time and position are continuous variables - Monte Carlo sampling is a natural choice
- Questions:
  - Can Monte Carlo transport help in continuous environment?
  - How much improvement can we expect if we include Monte Carlo dose calculation?

Continuous vs. discrete simulations

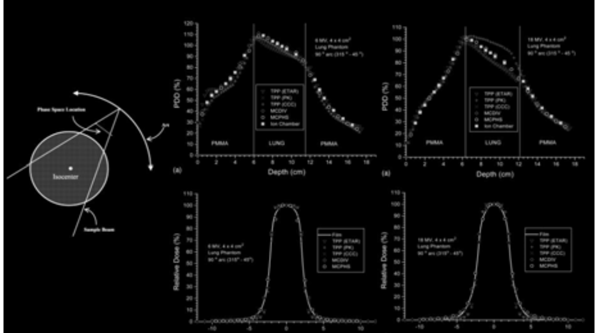


Phase space of discrete vs. continuous time-dependent helical tomotherapy simulations

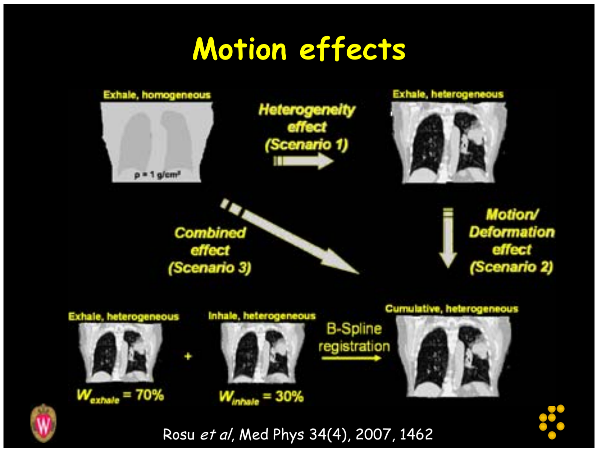
Tomotherapy delivery errors

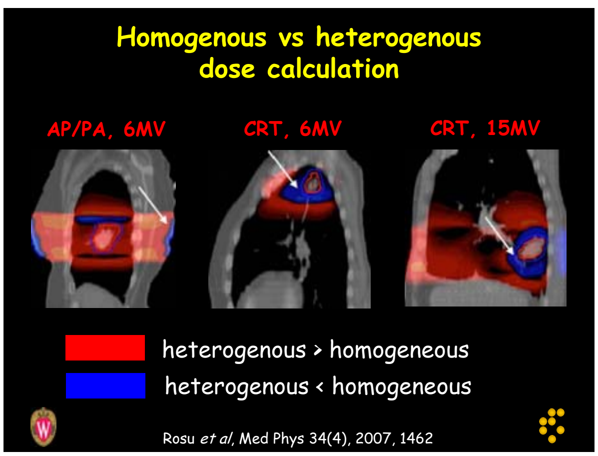


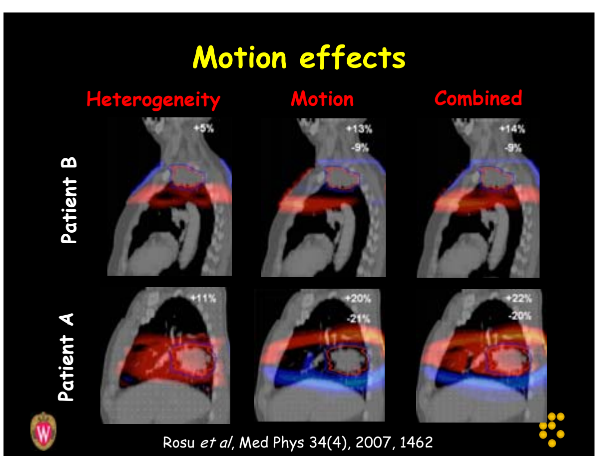
Arc therapy



Chow *et al*, Med Phys 30(10), 2003, 2686


Motion effects
Exhale, homogeneous
ρ = 1 g/cm³
Heterogeneity effect (Scenario 1)
Exhale, heterogeneous
Combined effect (Scenario 3)
Motion/ Deformation effect (Scenario 2)
Exhale, heterogeneous
Inhale, heterogeneous
B-Spline registration
Cumulative, heterogeneous
Wexhale = 70%
Winhale = 30%
Rosu et al, Med Phys 34(4), 2007, 1462


Homogenous vs heterogenous dose calculation
AP/PA, 6MV
CRT, 6MV
CRT, 15MV
heterogenous > homogeneous
heterogenous < homogeneous
Rosu et al, Med Phys 34(4), 2007, 1462

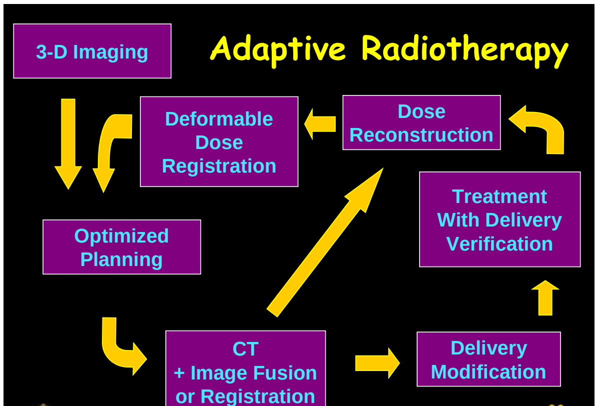

Motion effects
Heterogeneity
Motion
Combined
Patient B
Patient A
+5%
+13%
-9%
+14%
-9%
+11%
+20%
-21%
+22%
-20%
Rosu et al, Med Phys 34(4), 2007, 1462

Summary: Continuous MC simulations

- Monte Carlo simulations are ideal for continues simulations, both spatial and temporal
- Monte Carlo simulations not only account for continuous motion, but also properly for heterogeneities (need 4D-CT)
- Not much yet, but it will become very important in the future

Monte Carlo-based Adaptive Radiotherapy

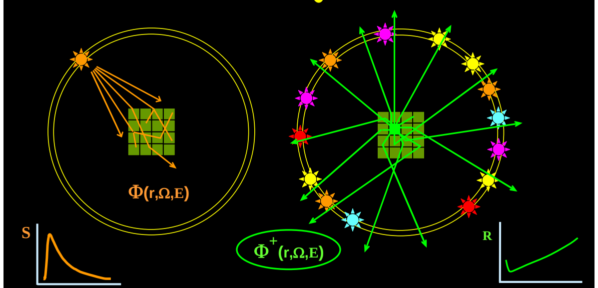
Adaptive Radiotherapy



Adaptive radiotherapy

- IGRT enables treatment adaptation
- Treatment adaptation is yet to happen
- Questions:
  - Can Monte Carlo transport help in adaptive process?
  - Can Monte Carlo transport help in re-optimization convergence?

Forward vs. adjoint method



$Dose = \langle \Phi,\ R \rangle$

$Dose = \left\langle \Phi^{+},\ S \right\rangle$

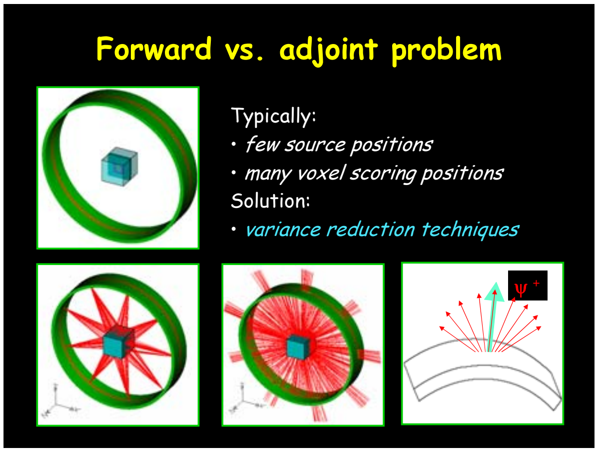
Forward vs. adjoint method

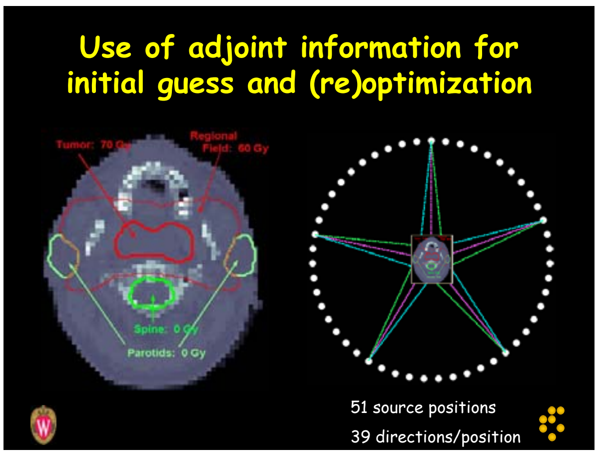
Forward Method

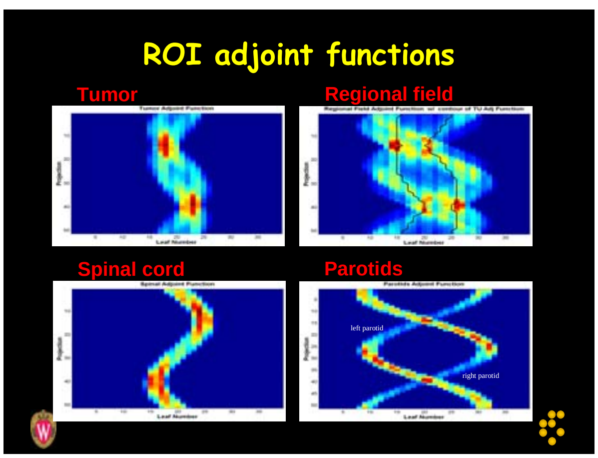
- Forward transport of the "source" function
- $\Phi\ (r,\Omega,E)$
- Q = $\langle \Phi, R \rangle$
- 1 source → many voxels (*source view*)
- Prior knowledge of the response function is unnecessary

Adjoint Method

- Backward transport of the "response" function
- $\Phi^{+}(r,\Omega,E)$
- Q = $\left\langle \Phi^{+}, S \right\rangle$
- 1 voxel → many sources (*voxel view*)
- Prior knowledge of the source function is unnecessary

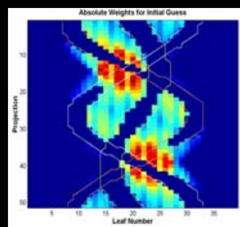

Forward vs. adjoint problem
Typically:
• few source positions
• many voxel scoring positions
Solution:
• variance reduction techniques
ψ +


Use of adjoint information for initial guess and (re)optimization
Tumor: 70 Gy
Regional Field: 60 Gy
Spine: 0 Gy
Parotids: 0 Gy
51 source positions
39 directions/position

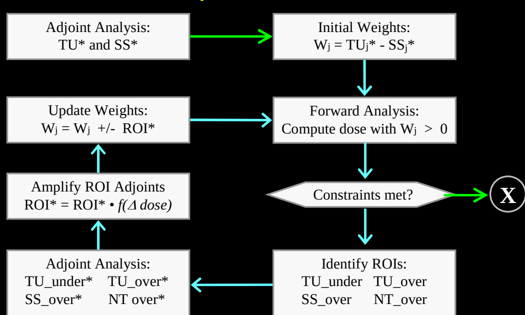

ROI adjoint functions
Tumor
Regional field
Spinal cord
Parotids
left parotid
right parotid

Initial guess: beam weights

- Determine relative importance of nonzero beams: $D^*_{TGT\,j} / \sum_j D^*_{TGT\,j}$
- Assign initial weights according to beam importance
- Reset zero-valued beams to value of least important beam

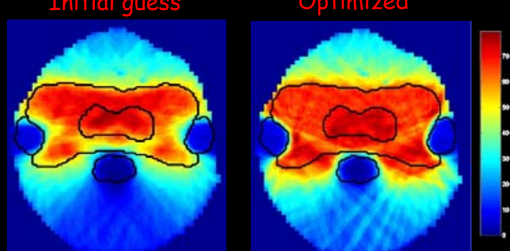


Use of adjoint information in re-optimization

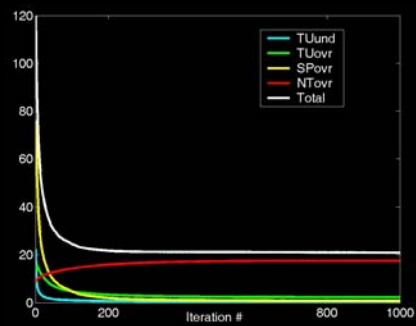


Iterative (re)optimization

Initial guess Optimized



Convergence



Adaptive radiotherapy

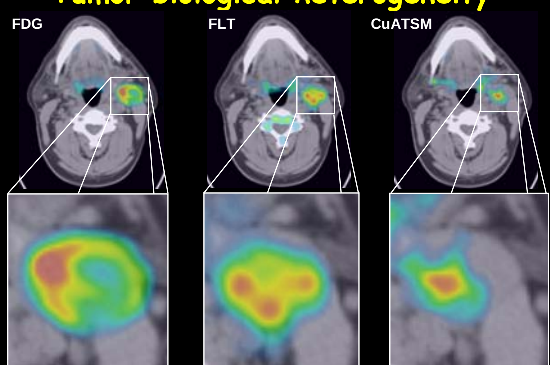
- Adaptive radiotherapy has yet to become clinical reality – many issues to overcome
- Adjoint Monte Carlo transport can:
  - Provide extremely valuable sensitivity information for adaptation
  - Help constructing initial guess
  - Improve optimization convergence
  - Can speed-up re-optimization

Monte Carlo-based non-Transport Applications

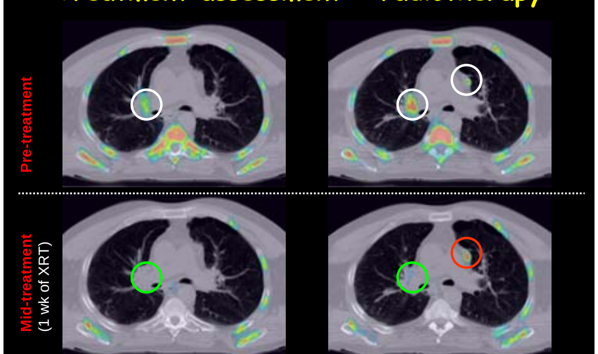
Do Monte Carlo simulations stop here

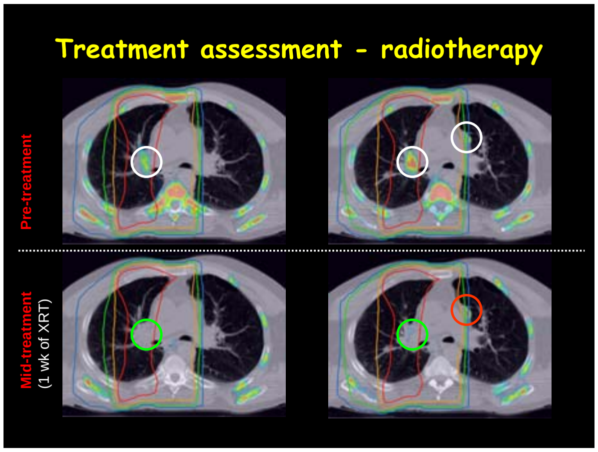
- Monte Carlo *transport* simulations are only a small part of Monte Carlo simulations
- Questions:
  - Is there a way to combine Monte Carlo transport with biological information available from functional/molecular imaging?
  - Is there a room for Monte Carlo non-transport applications?

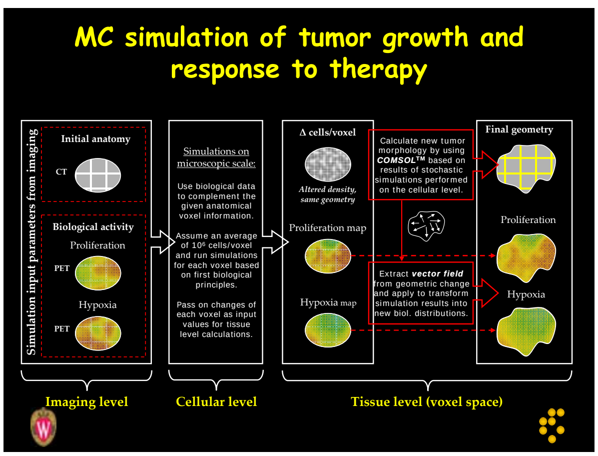
Tumor biological heterogeneity

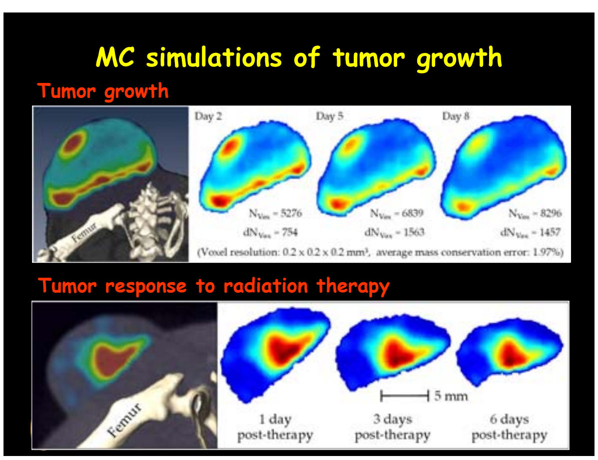


Treatment assessment - radiotherapy

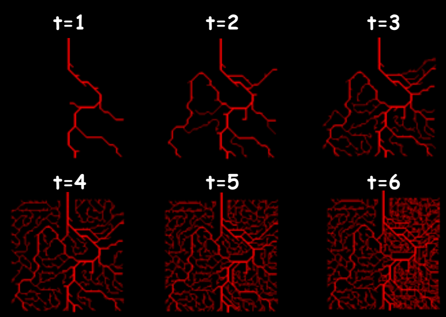



Treatment assessment - radiotherapy
Pre-treatment
Mid-treatment
(1 wk of XRT)


MC simulation of tumor growth and response to therapy
Simulation input parameters from imaging
Initial anatomy
CT
Biological activity
Proliferation
PET
Hypoxia
PET
Simulations on microscopic scale:
Use biological data to complement the given anatomical voxel information.
Assume an average of 10⁶ cells/voxel and run simulations for each voxel based on first biological principles.
Pass on changes of each voxel as input values for tissue level calculations.
Δ cells/voxel
Altered density, same geometry
Proliferation map
Hypoxia map
Calculate new tumor morphology by using COMSOL™ based on results of stochastic simulations performed on the cellular level.
Extract vector field from geometric change and apply to transform simulation results into new biol. distributions.
Final geometry
Proliferation
Hypoxia
Imaging level
Cellular level
Tissue level (voxel space)


MC simulations of tumor growth
Tumor growth
Femur
Day 2
Day 5
Day 8
N Vox = 5276
dN Vox = 754
N Vox = 6839
dN Vox = 1563
N Vox = 8296
dN Vox = 1457
(Voxel resolution: 0.2 x 0.2 x 0.2 mm³, average mass conservation error: 1.97%)
Tumor response to radiation therapy
Femur
5 mm
1 day post-therapy
3 days post-therapy
6 days post-therapy

MC simulations of vasculature growth



Conclusions

- Monte Carlo simulations will continue to play important role in the future
- Many new challenges and opportunities:
  - Characterization and optimization of (new) delivery systems – lots of opportunities, limitations
  - Imaging systems for IGRT – detectors, improved image quality (scatter)
  - Continuous treatments – underutilized right now
  - Adaptation – fast corrections/re-optimization
  - Non-transport/hybrid Monte Carlo applications – how far can we push the limit?

Thank you for your attention