Deformable Image Registration for Dose Accumulation

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Overview

1. Justification
2. Methods
3. Uncertainties
4. Applications to ART
5. Conclusions

1. JUSTIFICATION

The Beginning

- Historically, the dose accumulation tool emerged in conjunction with treatment planning in the presence of breathing motion to account for:
  - changes in anatomy prompted by respiration
  - subsequently induced dose variations
- Ultimate goal – describe more accurately the planned dose for the time-varying anatomy.
- In this context – dose accumulation is the process by which individual doses generated on datasets describing the anatomy at various respiratory phases are combined to create a composite dose.

More Anatomical Variations

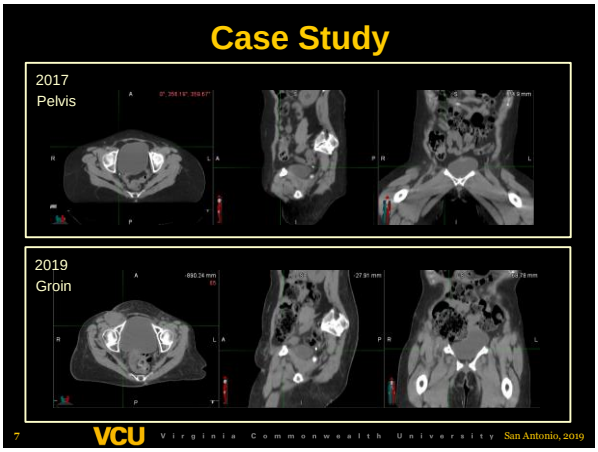
- Inconsistencies in patient anatomy due to other reasons (often less predictable):
  - weight loss
  - tumor shrinkage or growth
  - daily variations in:
    - relative organ positions
    - shape
    - volume
  - patient retreatments are often required, at times, years apart: real anatomical changes or changes due to setup occur.
- In all cases, properly accounting for prior doses is desirable in order to prevent:
  - damaging overexposure to organs at risk
  - tumor underdosage

A Little Bit of History

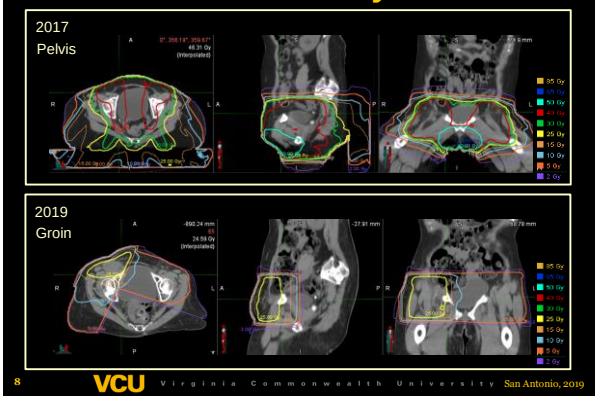
Approximate (usually conservative) paradigms have been long employed to estimate doses to critical organs from multiple treatments:

- Add maximum doses to OAR of interest.
  - Estimate maximum cord dose from two different treatment courses by adding maximum doses from each course, even though sometimes the regions of max dose did not overlap.
- "Rigid" superposition of doses.
  - Align anatomies rigidly in whatever meaningful way possible and sum up doses on a voxel-per-voxel basis.
- Downside –
  - Curative doses may, at times, be out of reach due to the overestimation of the dose to the uninvolved tissues.

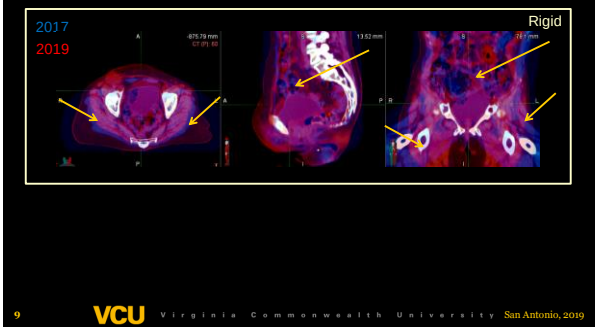
Case Study



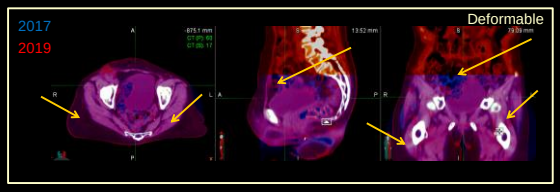
Case Study



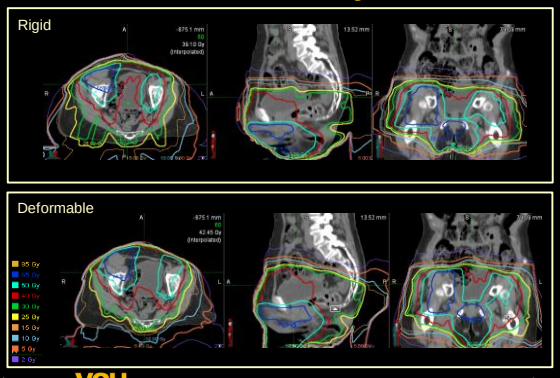
Case Study – Rigid Alignment



Case Study – Deformable Alignment



Case Study

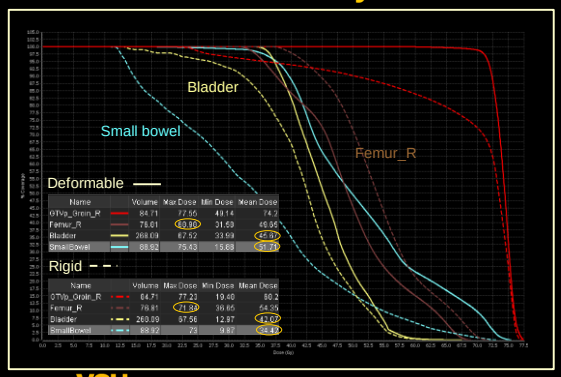


Case Study

Dose difference display between the rigid and deformable scenarios:

Large discrepancies cover extended areas, they are not just point differences.

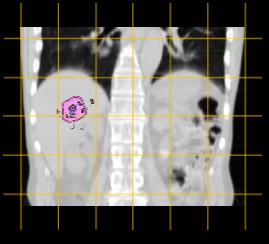
Case Study



2. METHODS

Anatomical Proxies

- Dose accumulation – Anatomical summation of dose distributions computed over multiple anatomical instances.

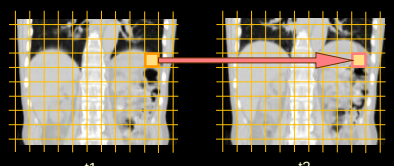


Ideally, one wants to track every minute anatomical entity.

Anatomy digitized by a mere computer → the voxels that make up the dose matrix are the proxies fulfilling the role of the tissue elements tracked over time.

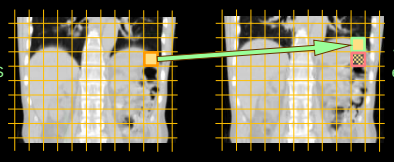
Geometrical vs. Anatomical Summation

Geometrical: Doses added between ANALOGOUS voxels



Voxels at the same location in the dose matrix.

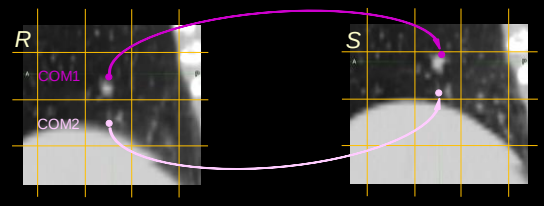
Anatomical: Doses added between HOMOLOGOUS voxels



Voxels that encompass the same anatomy.

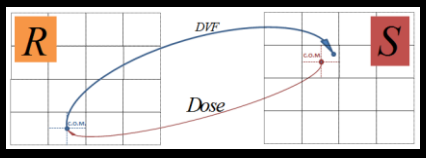
Zooming In

- Adding doses to homologous entities is an intuitive concept.
- Complicated due to voxelized nature of the data.



- Voxels characterized by a unique location - COM.
- By means of image registration, COM from *R* can land anywhere inside a dose grid voxel from *S*, even together with other voxel centers.

COM Method



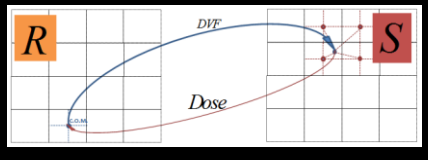
- Track the COM.
- The COM method was implemented in the Geant4 Monte Carlo code and demonstrated for a proton lung cancer irradiation case by Paganetti et al, 2004*.
- *R* voxel COM mapped on the secondary dataset.
- It will get assigned the dose from the COM of the *S* voxel where it landed, and then will be accumulated to *R* voxel.

*Paganetti H et al. Monte Carlo simulations with time-dependent geometries to investigate effects of organ motion with high temporal resolution. Int J Radiat Oncol Biol Phys 60:942-950, 2004.

COM Method

- Most direct way to calculate the dose that a voxel from *R* dataset will receive from the dose grid computed on *S* dataset.
- Major advantage:
  - Can be used with any dose calculation algorithm – only quantity involved is the COM dose in both *R* and *S* datasets, regardless of the algorithm used to compute it.
- Shortcomings:
  - Voxel shape/volume changes from one image set to another are not explicitly addressed.
  - Physical aspects of dose deposition are left out.

Tri-linear Interpolation

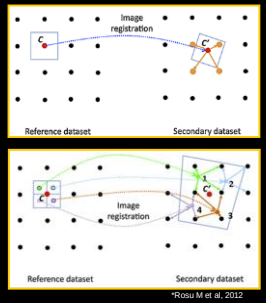


- The COM of *R* dose voxel mapped on *S* dataset lands almost certainly away from any COM.
- Its dose can be approximated by trilinear interpolation of the doses to the neighboring voxels.
- Fast.
- Can be used with any dose calculation algorithm.
- Ignores the physical aspects of dose deposition as energy per mass.

*Schaly B et al: Tracking the dose distribution in radiation therapy by accounting for variable anatomy. Phys Med Biol 49:791-805, 2004.
Rosu M et al: Dose reconstruction in deforming lung anatomy: Dose grid size effects and clinical implications. Med Phys 32:2487-2495, 2005.

Finer Tri-linear Interpolation

- Finer trilinear interpolation can be used if larger local deformations are present.



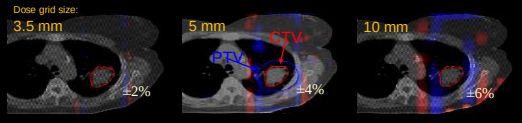
*Rosu M et al, 2012

- Each *R* voxel is subdivided into octants.
- Center of each octant mapped to locations on the *S* dose grid.
- Doses at the tracked locations are estimated by trilinear interpolation.
- Their average values are scored at the *R* dose grid point locations.
- Does the dose grid size matter?

Relative Dose Grid Size Effects

Differences in doses received by exhale voxels at inhale:

Refined linear approximation – Direct linear approximation

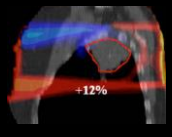


Differences between the interpolation schemes:

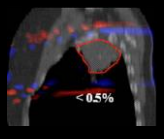
- Primarily in steep dose gradient regions.
- Voxel size dependent, increase as the voxel size increases.
- Unlikely to result in clinically significant differences for volume-effect organs (eg, lung tissue).
- Should be viewed more carefully for serial organs (eg, spinal cord) with consideration of tumor location, magnitude of deformation, motion, and tissue heterogeneity.

Dose Grid Size Effects

Change in the dose when mapped from exhale to inhale (3 mm grid)



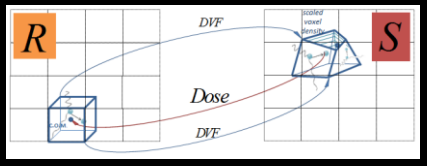
Differences between exhale-mapped-to-inhale doses for 3 and 10 mm grid sizes



- The magnitude of the differences between the two interpolation schemes is typically less than the alteration in doses due to positional and shape changes from breathing in the first place.
- The use of the refined interpolation is not necessarily equivalent to the use of the direct method at a finer grid resolution because the larger dose calculation grid inherits erroneous voxel dose estimation in the first place.

Direct Voxel Tracking Method

(Voxel Warping Method)



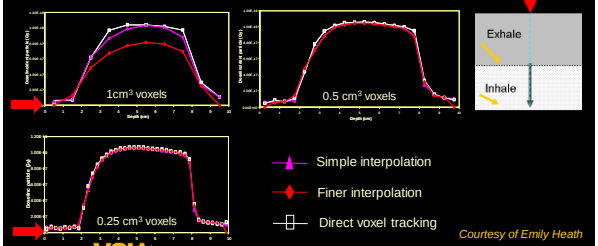
- Monte Carlo calculations account for the physical aspects of dose deposition.
- Due to deformations, rectangular voxels from *R* become of an arbitrary shape on *S*.
- Particle transport in *S* is performed inside deformed voxels.
- Deformed voxel densities adjusted to ensure mass conservation.
- Energy deposited in the given mass of tissue is computed and mapped on *R*.

*Heath E, Seuntjens J: A direct voxel tracking method for four-dimensional Monte Carlo dose calculations in deforming anatomy. Med Phys 33:434-445, 2006.

Direct Voxel Tracking Method

Discrepancies between the voxel tracking and the trilinear interpolation method – larger differences:

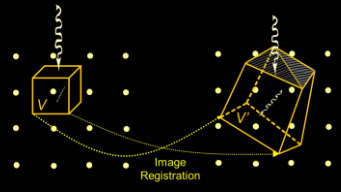
- regions of steep dose gradients
- entrance and distal surfaces of the study phantom
- large voxel sizes (1 cm)



Courtesy of Emily Heath

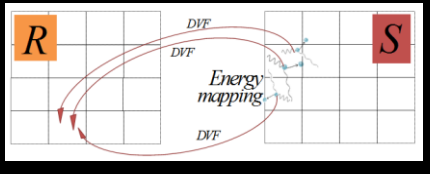
Direct Voxel Tracking Method

- Computationally expensive (~10 times larger than regular DOSXYZrnc calculation)
  - each "face" of the deformed voxel approximated with 2 planes, forming dodecahedrons
    - number of distance-to-voxel boundaries to be verified is doubled
    - additional testing is necessary to ensure that the particle-plane intersections occur inside the deformed voxel boundary



In a subsequent implementation, each deformed voxel divided in 6 tetrahedrons for dose transport, substantially decreased the computation time.

Energy Transfer Method

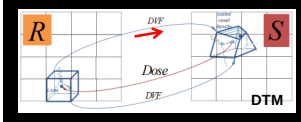


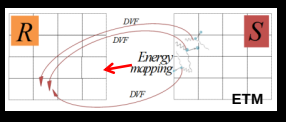
- Energy deposition events simulated in *S* on standard rectangular grid …
  - Removes the computational hardship of transporting particle within irregular boundaries.
- … then mapped onto *R*.
- Dose to a voxel from *R* was computed as the energy mapped from *S* divided by the mass of the *R* voxel.

Siebers JV, Zhong H: An energy transfer method for 4D Monte Carlo dose calculation. Med Phys 35:4096-4105, 2008.

DTM vs ETM in a nutshell

- The Dose Tracking Method (DTM) and the Energy Transfer Method (ETM) differ in:
  - information mapped
  - particle transport





- Maps *R* dose grid voxel on *S*
- Computes dose in an irregularly shaped voxel on *S*
- Scores *S* dose on *R*

- Simulates particle transport in *S* to compute energy deposition
- Maps *S* energy deposition on *R*

Note the opposite directions of the DVFs needed in the two methods.

3. UNCERTAINTIES

Uncertainties

- We have ways to merge dose distributions using the powerful tool of image registration,

  …**"but let us not be so naïve as to believe we have achieved our goal of ultimate accuracy"***

- Factors influencing the accuracy of deformable dose accumulation:

  A. Registration (DVF) inaccuracies

  B. Summation of doses for different fractionation regimens

  C. Tissues that change mass

The ultimate problem in evaluating cumulative doses is the lack of ground truth, which makes any attempt to quantify its uncertainty only hypothetical.

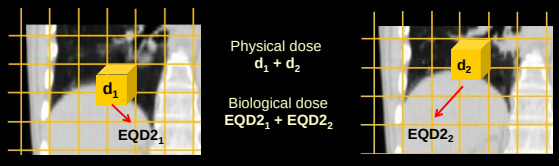
*Schultheiss TE, Tome WA, Orton CG: Point/counterpoint: It is not appropriate to "deform" dose along with deformable image registration in adaptive radiotherapy. Med Phys 39:6531-6533, 2012.

A. Dose Uncertainty Estimation

- Measure the deformed dose distribution by embedding dosimeters in the patient's body – *invasive and impractical*.
- Compare calculated dose accumulation to measurements in a deformable phantom – *direct clinical applicability of phantom tests is limited due to insufficient complexity of phantom design to match that of patient anatomy.*
- Evaluate DVF uncertainty from mechanical or mathematical properties of the deformation and translate them to dose mapping – *results will depend on the registration algorithm used.*
- Estimate the mean and variance of DVF errors from measured data and then blur dose maps – *requires making assumptions about the spatial properties of the errors.*
- Create a distribution of DVF maps, perturb a dose mapping by the DVF error map and observe the statistical distribution of dose mapping errors that arises from the statistical distribution of DVF errors – *not clinically feasible at this time.*
- Evaluate inverse consistency error and correlate it with dose mapping accuracy – *not clinically feasible at this time.*

B. Different Fractionations

- In the case of re-irradiation, different fractionations may be used.
- Typically, dose summations neglect the biological effect of dose per fraction.
- Boman et al* summed doses as 2 Gy equivalent doses (EQD2) resulting from deformable registration of retreatments:



Dose per fraction for each voxel is converted to EQD2.
EQD2 doses summed per voxel.

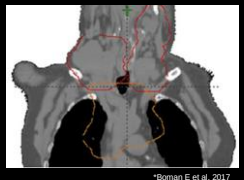
*Boman E, Kapanen M, Pickup L, et al: Importance of deformable image registration and biological dose summation in planning of radiotherapy retreatments. Med Dosim 42:296-303, 2017.

B. Different Fractionations

Example case:

PTV1 20 Gy (5 × 4 Gy), arms up
PTV2 30 Gy (10 × 3 Gy), arms down

A few centimeters overlap between *PTV1* and PTV2.



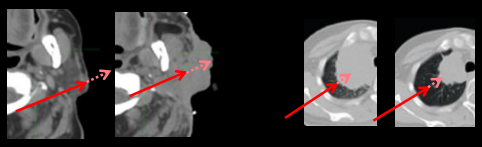
*Boman E et al, 2017

Organ/Parameter	Def Physical sum	Def Biological sum
Medulla D0.1cc (Gy)	33	35
Esophagus D0.1cc (Gy)	50	63
Esophagus D50% (Gy)	50	63
Esophagus mean (Gy)	46	56

Cumulative doses may vary by a significant factor when deformable image registration and biological dose summation are used.

C. Tissue That Changes Mass

- Tissue spatial changes that image registration cannot account for:



- Most DIR algorithms use image intensity similarity measures.
- Deformation tends to align border of tumor mass, as if a tissue compression or expansion occurred – not correct.

Best, for now, for such scenarios:
Use local rigid mapping to estimate doses in the aligned area.

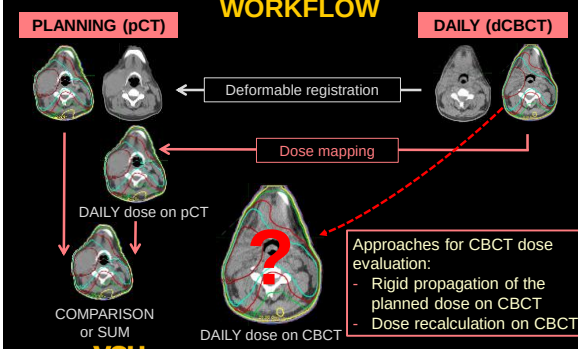
4. APPLICATION TO ART

Adaptive Radiation Therapy

- The contemporary ART aims at using daily images to update the patient model and evaluate the dose-of-the-day.
- The concept was stimulated by the availability of in-room volumetric imaging which is routinely used for patient setup verification.
- Attractive because in-room CBCT provides an updated daily snapshot of the patient model assumed at planning.

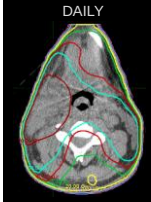
Adaptive Radiation Therapy

WORKFLOW



Approaches for CBCT dose evaluation:
- Rigid propagation of the planned dose on CBCT
- Dose recalculation on CBCT

Rigid Propagation of Planned Dose



Underlying assumption:

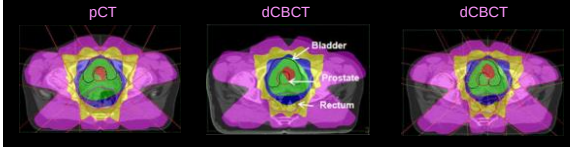
Dose distribution in an accelerator coordinate system is invariant to small changes of the anatomy placed in the field.

↓

Planned dose can be transferred rigidly on the daily image, based on the daily alignment coordinates.

- Fast method!
- Contours needed on the dCBCT to evaluate the relevant metrics – may not necessarily be an easy task given the poor CBCT quality.

Rigid Propagation of Planned Dose



Planned dose

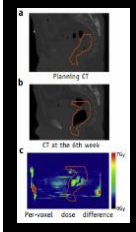
Planned dose aligned with treatment isocenter on the daily image

Dose recalculated on the daily image at the treatment isocenter

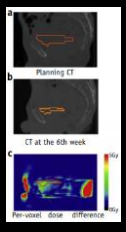
- The assumption of dose invariance seems justified in this example, possibly because an "empty bladder and rectum protocol" was followed, resulting in smaller daily anatomical variations.
- Differences in general < 2%.

Sharma M, Weiss E, Siebers J: Dose deformation-invariance in adaptive prostate radiation therapy: Implication for treatment simulations. Radiother Oncol 105:207-213, 2012.

Rigid Propagation of Planned Dose



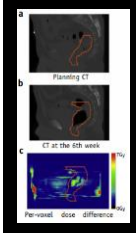
- Larger differences in cases were larger anatomical variations existed. ~ 4 Gy bladder and rectum
- For the entire population, the mean difference was
  - < 0.5 Gy for 70% of the patients for the whole bladder
  - < 0.5 Gy for 65% of the patients for rectum



Rectum and the gas volume variations ← These descriptors may be screened to evaluate the need for dose recalculation. → Bladder and external contour variations

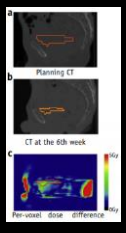
Simon A, et al: Dose deformation invariance hypothesis verified in prostate IGRT. Int J Radiat Oncol Biol Phys97(4):830-838, 2017.

Rigid Propagation of Planned Dose



If a mean per-voxel dose difference higher than 1 Gy is assumed clinically relevant –

Dose recalculation in < 15% of the fractions.



Simon A, et al: Dose deformation invariance hypothesis verified in prostate IGRT. Int J Radiat Oncol Biol Phys 97(4):830-838, 2017.

Dose Recalculation on CBCT

- Not trivial to calculate dose directly on CBCT:
  - Poor quality, affecting ability to align it with the planning CT and to do dose calculations.
  - Relatively short length, may not encompass the entire anatomy.

Reason for poor CBCT image quality:

- Large volume of the patient is simultaneously irradiated.
- Large amount of scatter created which negatively impacts the contrast and is a source of artifacts.

- CBCT images do not necessarily provide correct HU, thus cannot be confidently used for the dose calculation.
- Relationship between HU units and the attenuation coefficient of the patient's tissues will be patient-dependent.

Techniques for Dose Recalculation

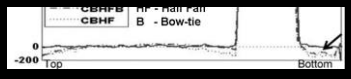
- Standard CBCT HU calibration curve
- Site-specific CBCT HU calibration curve
- HU override
- pCT to dCBCT density override

Standard Calibration Curves

HD calibration tables are generated from phantom measurements.

HU profiles in inhomogeneous phantom*:

Phantom-based calibration curves for CBCT are not robust enough to be used for all patients and all anatomical locations.



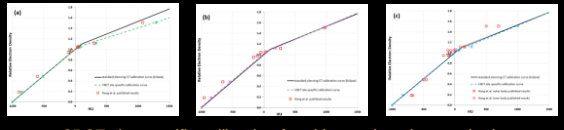
- HU profiles from CBCT scans exhibit larger inaccuracies when inhomogeneities are present (~300 Hus), adequate otherwise.
- Recommendation: CBCTs acquired with bow-tie filter if the scan will be used for treatment planning.

Yoo S and Yin FF: Dosimetric feasibility of cone-beam CT-based treatment planning compared to CT-based treatment planning. Int J Radiat Oncol Biol Phys 66(5):1553-1561, 2006.

Site-Specific Calibration Curve

- A refined phantom calibration method by Giacometti et al* used additional scatter material in the phantom to more accurately simulate a patient's tissue composition.
- Results for standard CT HU curve, standard phantom CBCT HU and modified phantom CBCT HU curves:

CT Standard calibration | CBCT Standard calibration | CBCT Modified phantom

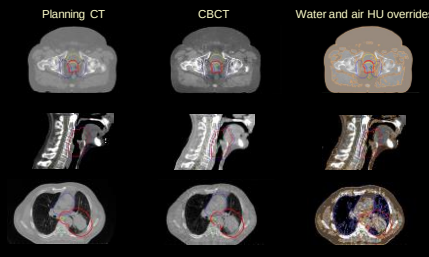


- CBCT site-specific calibration fared better than the standard CBCT calibration when compared to the CT calibration.

Giacometti et al: An evaluation of techniques for dose calculation on cone beam computed tomography. Br J Radiol 92: 1096, 2018.

HU Override

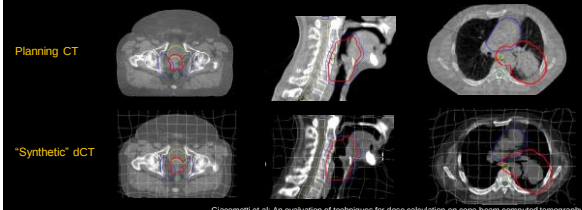
- Several tissues (air, lung, adipose, muscle, soft and dense bone and metal) are delineated (autocontoured) on the CBCT images.
- HU override values for these structures are determined from corresponding volumes autocontoured on the patient's planning CT.



Giacometti et al: An evaluation of techniques for dose calculation on cone beam computed tomography. Br J Radiol 92: 1096, 2018.

pCT to dCBCT Density Override

- dCBCT images are non-rigidly registered with pCT.
- pCT image is deformed to match the dCBCT image.
- A "synthetic" dCT is created, resembles dCBCT morphologically, but has dCT HU values.
- When necessary, CBCT images may be "patched" with data from CT to extend the length of their FOV.



Giacometti et al: An evaluation of techniques for dose calculation on cone beam computed tomography. Br J Radiol 92: 1096, 2018.

pCT to dCBCT Density Override

- Advantages:
  - Avoids, in part, issues associated with inaccurate HU values.
  - Avoids the negative impact of CBCT artifacts on calculated dose distributions.
  - *Bonus*: facilitates the propagation of the outlined structures from pCT to dCBCT as a starting point in contouring (easier than contouring from scratch).
- Disadvantages:
  - Registration may not perform sufficiently well across the entire anatomy of interest –
    - One needs to prioritize what anatomical regions are of utmost importance.
  - Does not address potential daily changes in tissues densities from their values when the pCT was acquired.
  - Registration accuracy cannot be evaluated
    - In detail
    - Accurately

5. CONCLUSIONS

Closing Statements

Should deformable dose accumulation be deployed routinely in the clinic?

- The tools exist, but their uncertainty and how the uncertainty affects the results is still not a settled issue.
- Moreover, the ground truth is out of reach, and visual validation is still the ultimate verification modality.
- We are surely far ahead from where we were just a few years back!

Closing Statements

Should deformable dose accumulation be deployed routinely in the clinic?

Even though dose accumulation is not worry free yet,
we should continue to put it to work
(albeit cautiously)
because it is the only way to make strides on the
learning curve.

Thank you!