Image Registration in Treatment Planning

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Outline

- Introduction
- Informatics
- Algorithms
- Specific Modalities
  - MR
  - PET
  - 4DCT
- Deformable Registration

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Introduction

- Why image registration between the same or multi-modalities is needed

Spatially
- Anatomical information
- Physiological information
- Dosimetric information

Temporally
- Motion
- Retreatment response
- Daily/fractional dose

All these information may need to be combined with planning CT for

Target/organ delineation
Motion assessment
Adaptive re-planning
Outcome evaluation

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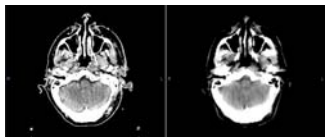
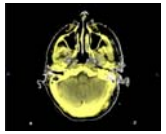
Registration & Fusion

- Registration
  - Transformation of the coordinate system of one image to that of another.
- Fusion
  - Display of two merged images.





The two terms are often used interchangeably .

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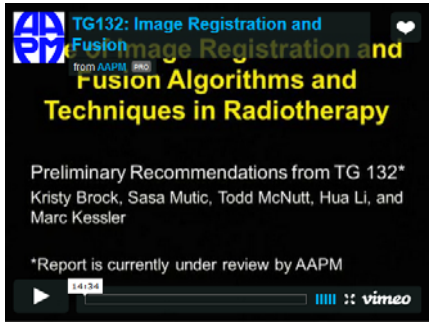
Upcoming AAPM TG-132 Report

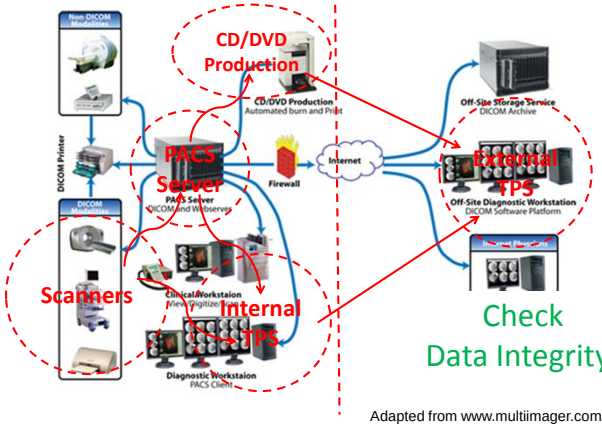


Brock *et al*. Presented at AAPM 2013. Recording available at aapm.org for AAPM members.

Informatics

- Access to multi-modality images
- Appropriate handling of DICOM format

Access to multi-modality images



Check Data Integrity!

Adapted from www.multiimager.com/pacs.htm

"DICOM Problems"

- Patient/image orientation not recognized
- MR slices titled
- "They sent us some screenshots in DICOM format!"
- TPS refuses to perform registration!

And many many more!

Patient/Image Position and Orientation

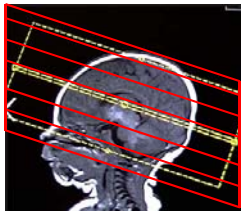
- Patient Position (0018,5100)
- Image Orientation (Patient) (0020, 0037)
- Image Position (Patient) (0020, 0032)

etc.

It is not uncommon to see software bugs related to uncommon use of Patient/Image position and orientation.

MR Slices Tilted

- The native MRI slices can be tilted relative to the scanner.

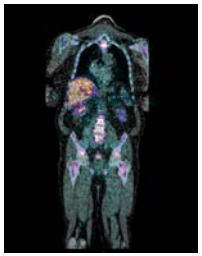


From: www.mrimaster.com

A lot of software cannot handle it.

"Screenshot" DICOM Images

- Some imaging systems burn screenshots (*with all good intention*) into CD/DVD in DICOM format for external requests.
  - RT Image Conversion Type (0008, 0064): WSD



Images in the Same Frame of Reference

- Images in the same "Frame of Reference" (0020, 0052) are explicitly registered already; some TPS refuses to perform further registration between them.

You may manually make them different by editing this DICOM tag, but be careful of losing its registration with other images.

No Software Has Handled All Situations Correctly

- Occasional DICOM editing may be necessary.
  - At least we can find what is wrong with the images.

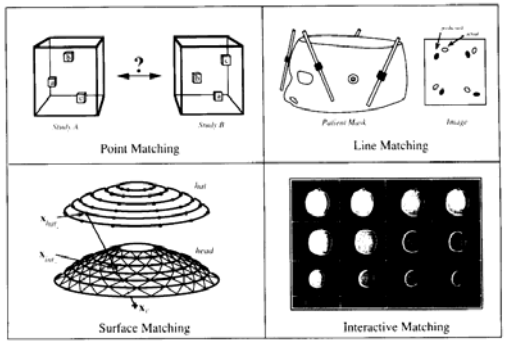
My favorite: DicomEdit.

Image Registration Methods

- Landmark-based (e.g., fiducial marker or anatomic landmark)
- Segmentation-based
- Voxel property-based
  - Chamfer matching (edge matching)
  - Cross correlation
  - Mutual information (reduction of joint entropy)

Suggested Reading: Maintz and Viergever. "A survey of medical image registration" 1998. Medical Image Analysis 2:1-36. (cited >3,000 times)
Kessler. "Image registration and data fusion in radiation therapy" 2006. British Journal of Radiology 79: S99-S108.

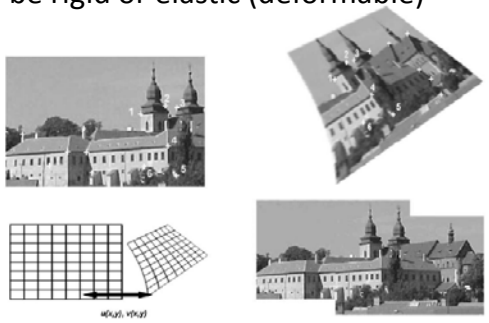
Image Registration Methods



Kessler et al. 1991. "Integration of multimodality imaging data for radiotherapy treatment planning". Med Phys. 21:1654-1667.

Landmarked-based Registration

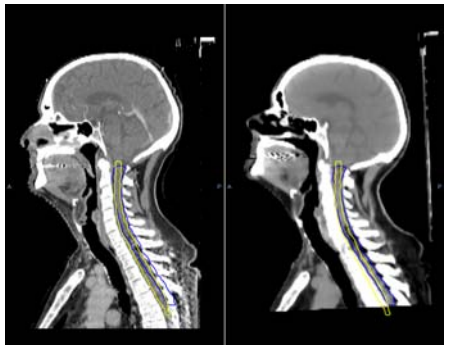
- Can be rigid or elastic (deformable)



From: Zitova and Flusser. "Image registration methods: a survery" 2003. Image and Vision Computing. 21:977-1000.

Segmentation-based Registration

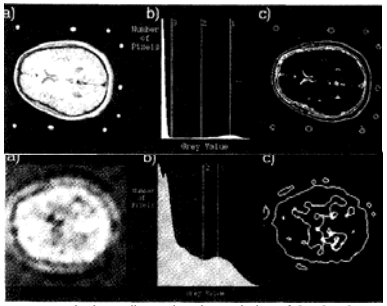
- Rigid or elastic
- Mostly by matching surface of the structure



This example tries to match the spinal cords in the two images.

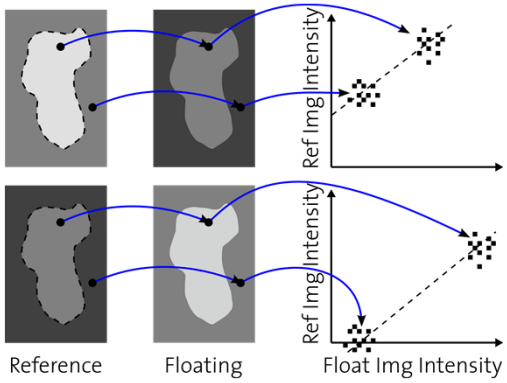
Chamfer Matching

- Extract edges (or line features) in the images, and minimize their distances.



Van Herk and Kooy. "Automatic three dimensional correlation of CT-CT, CT-MRI, and CT-SPECT using chamfer matching. 1994. Med Phys 21:1163.

Cross Correlation



Courtesy of Dr. Cattin. http://miac.unibas.ch/BIA/04-Registration.html

Mutual Information (Joint Entropy)

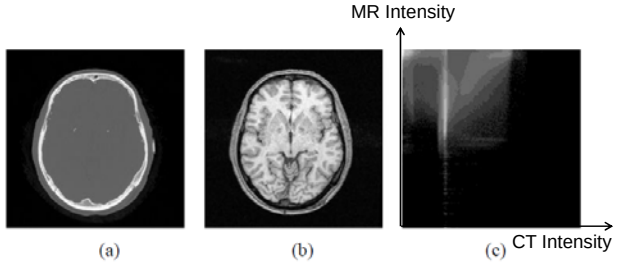


Figure c) is the joint intensity histogram, where each point represents the probability of a CT-MR intensity pair. The optimization of image registration is to minimize the entropy of the joint histogram.

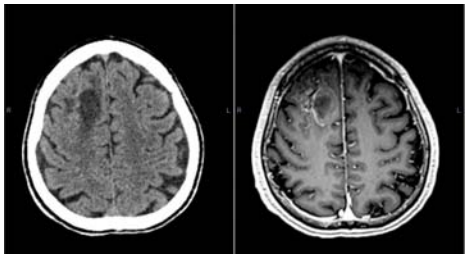
Maes et al. "Multimodality image registration by maximation of mutual information". 1997. IEEE Trans Med Imag 16:187-198.
Pluim, Maintz, Viergever. "Mutual-information-based registration of medical images: a survey". 2003. IEEE Trans Med Imag. 22:986-1004.

MR/PET/4DCT → CT Registration

- Clinical values
- Considerations in clinical application
  - Where to register: bone, tumor, a specific ROI?
  - How do they help target definition?
  - How big is the uncertainty?
- UIHC Example

MR in Radiation Therapy

- Clinical Values:
  - Better soft-tissue contrast for target delineation

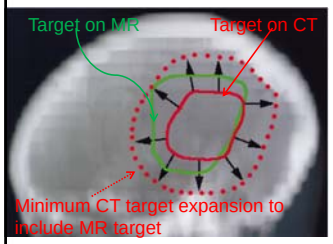


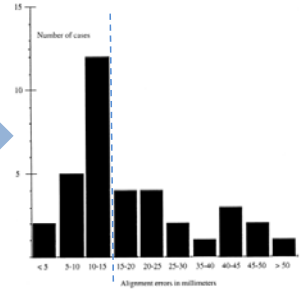
  - May also be used to obtain physiological or functional information in MR spectroscopy or with perfusion, defusion, etc.

MR in Radiation Therapy

- Disadvantages:
  - Lack of signal from bone; not possible to distinguish air-bone boundary
  - Geometrical distortion
  - No electron density information
  - Intensity variation across image
  - May not be scanned at treatment position
- Not ideal for localization or dose computation.

MR-defined Target is Necessary



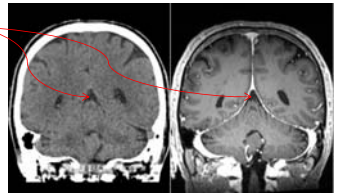


A 1.5cm expansion is not sufficient for 50% of the cases.

Rosenman et al. 1998. "Image registration: an essential part of radiation therapy treatment planning". IJROBP 40:197-205.

MR-CT Registration Methods

- Brain
  - Landmark-based registration
    - Tentorium cerebelli
    - Eye balls
    - Inner ear canals
  - Check:
    - Brainstem
    - Cerebrospinal fluid (CSF)
  - Make sure:
    - Visible tumors overlap
  - <1 voxel accuracy achievable



Clinical Sites using MR in Treatment Planning

- Brain
- Extremities
- Abdomen/Pelvis
  - Liver, kidney
  - Cervix
  - Prostate
- Head & Neck

Always a physician's call based on clinical context.

MR-CT Registration

- Question: **Do you register to bone, or to soft tissue?**
  - They are the same for brain or extremities (most of the time);
  - Discrepancies exist between MR and CT organ positions and shapes;
  - Minimize the time lapse between MR and CT and keep patient positioning consistent.
- Answer: **Depends on what you need**.

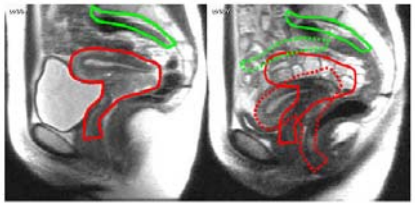
MR-CT Registration

- Pelvis as an example

  -Align to bones (at the axial level of primary target)

  -Be aware of organ discrepancies and whether they are reproducible during Tx
  - **Create ITV**

  or
  - **Align to tumor**



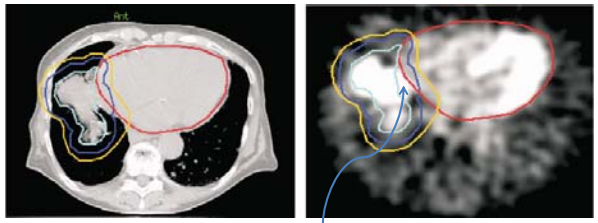
Lim et al. 2011. "Consensus guidelines for delineation of clinical target volume for intensity-modulated pelvic radiotherapy for the definitive treatment of cervix cancer." IJROBP. 79:348-355.

^{18}FDG-PET in Radiation Therapy

- ^{18}FDG for tumor detection
  - The only widely reimbursable PET agent
  - FDG is a glucose analog; activity corresponds to metabolism
  - Identifies cancer cells (primary, nodal, metastatic)
  - Mostly taken as a whole-body scan with attenuation correction (AC) CT.
- Many other PET agents exist
  - ^{18}FLT-PET; activity corresponds to cell proliferation

FDG-PET for Lung Target Definition

- Use of FDG-PET changes the GTV and nodal involvement



GTV contoured on CT does not fully cover the "tumor" detected on PET.

Erdi et al. 2002. "Radiotherapy treatment planning for patients with non-small cell lung cancer using positron emission tomography" Radiother Oncol. 62: 51-60.

FDG-PET for Lung: RTOG 0515

Bradley et al. 2012. "A phase II comparative study of gross tumor volume definition with or without PET/CT fusion in dosimetric planning for non-small-cell lung cancer (NSCLC): primary analysis of Radiation Therapy Oncology Group (RTOG) 0515.". IJROBP. 82:435-441.

Conclusion: "PET/CT-derived tumor volumes were smaller than those derived by CT alone. PET/CT changed nodal GTV contours in 51% of patients. The elective nodal failure rate for GTVs derived by PET/CT is quite low, supporting the RTOG standard of limiting the target volume to the primary tumor and involved nodes."

FDG-PET for Other Sites

- Head & neck; cervical
  - Detection of nodal disease and distant metastasis
- Esophageal; anorectal
  - Identifying primary tumor, as wall thickening not indicative of tumor extent
- During and after treatment: monitoring of tumor response

Practical Considerations for PET/CT

- Small uncertainty if the attenuation correction CT (AC-CT) in PET can be used as the simulation CT.
  - Positioning and immobilization device
  - Flat couch top
  - Timing between CT and PET scan and scan direction
- If AC-CT is not the simulation/planning CT, efforts are needed to minimize the their differences.

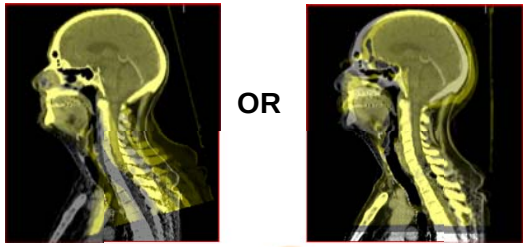
PET-CT Registration

- When AC-CT is not Planning CT
  - PET → Planning CT (large uncertainty)
  - PET → AC-CT → Planning CT

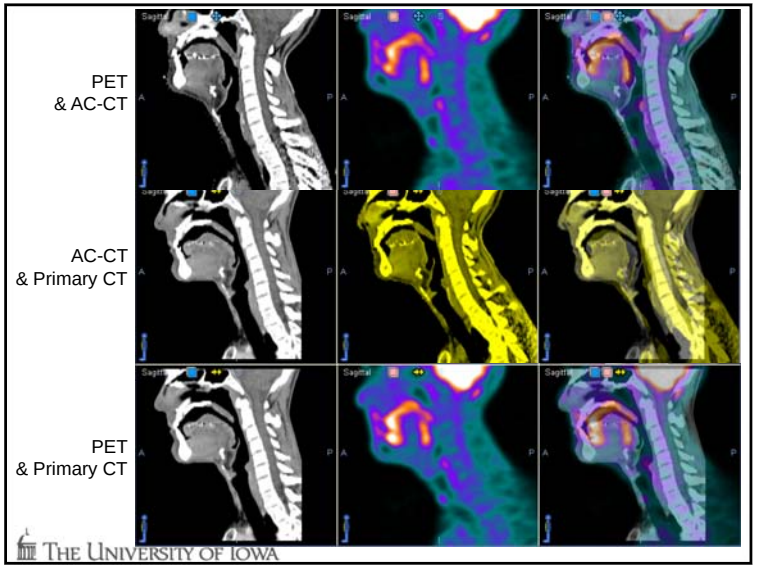
Clinical Considerations

- Where to focus?
- How to define target volume considering the registration uncertainty?

PET-CT: Where to Register?



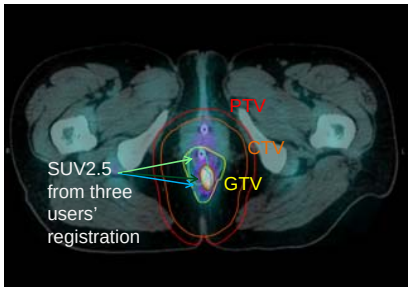
- Focus on the high uptake region
- Use visual correlation



PET-CT: Target Definition

- Make sure physician is aware of the uncertainty in PET-CT registration
- Typically target volume is large enough to cover the uncertainties

SUV2.5 is for reference only; it is not the target itself.



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4DCT to Planning CT

- Question (again): **Do you register to bone, or to organs?**
  - To get motion information from each phase, register to bone.
  - To contour target on each phase, register to organ/tumor (especially for liver or adrenal lesion when 4DCT has very low SNR)

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An Multi-modality Image Registration Example

- Case: Liver SBRT
- Planning CT: Exhale breath-hold CT
- Secondary datasets:
  - Inhale breath-hold T1 MR
  - Exhale breath-hold T1 MR
  - 4DCT
  - FDG-PET & AC-CT from Radiology 6 days ago

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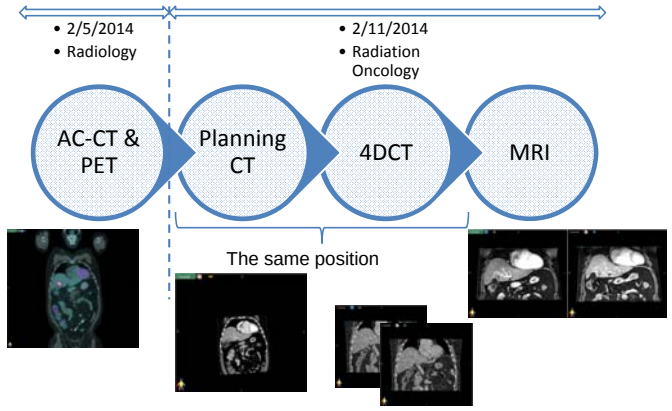
Liver SBRT Example – Imaging Timeline



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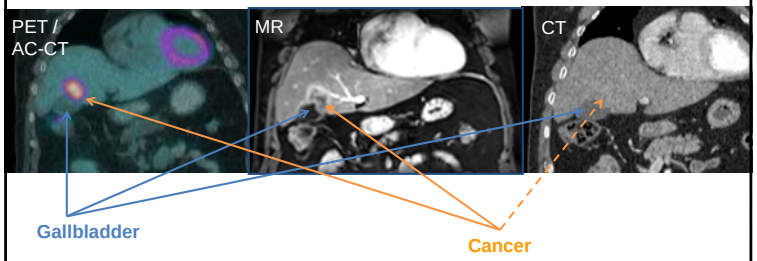
Liver SBRT Example

- Step 1. Physician visually inspects the correlation between PET and MR, then contours GTV on MR.



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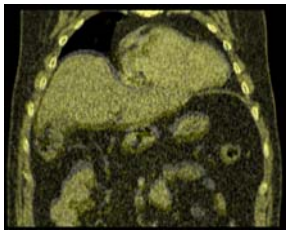
Liver SBRT Example

- Step 2. Physicist analyzes 4DCT images and determines 1). whether gating is needed; 2) the 4DCT phases used for planning.



Different phases of 4DCT are co-registered to the same Frame of Reference; no manual registration is needed.

0%Exhale-100%Inhale covers full range of motion, which is less than 1 cm.

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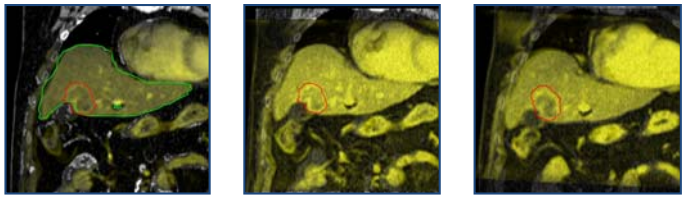
Liver SBRT Example

- Step 3. Dosimetrist registers MR to planning CT as well as 4DCT of 0% Exhale and 100% Inhale phases by *matching liver*, and maps the GTV to each CT.



Planning CT & Exhale MR | 0%Exhale CT & Exhale MR | 100%Inhale CT & Inhale MR

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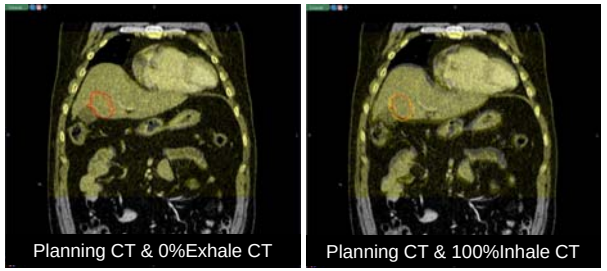
Liver SBRT Example

- Step 4. Dosimetrist registers 4DCT of 0%Exhale and 100%Inhale phases to planning CT by *matching bony anatomy*, and combine GTVs of all three CT images into ITV.



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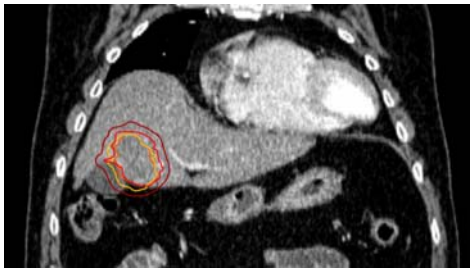
Liver SBRT Example

- Step 5. Physician reviews the registrations, GTV on different images, ITV, and creates PTV by expansion.



Planning CT

Summary on Rigid Registration

- MR and PET has clinical values in treatment planning;
- Whether to register to bone or tumor/organ depends on the needs;
- Make sure physician is aware of the registration uncertainty.

Clinical Deformable Image Registration in Treatment Planning

The University of Iowa Experience

June 2012 - March 2014

Dongxu Wang, PhD

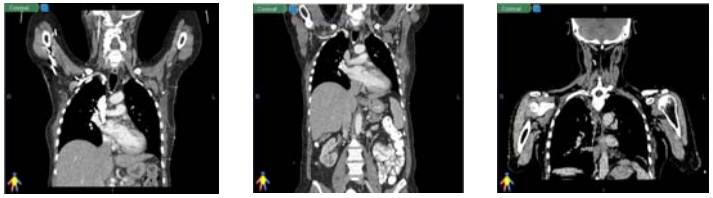
Conflict-of-Interest

None.

Disclosure: We use VelocityAI v2.8.1 clinically, and have a non-clinical version of RayStation v4.0 for research use.

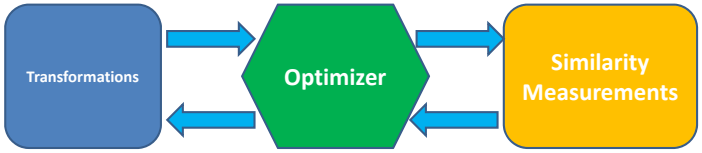
Deformable Image Registration - Assumption

- Human body may "deform", but it is still the same person.
- Assumption: there exist a point-to-point correlation between images of the same patient.

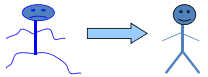


11/2010 3/2013 3/2014

Deformable Image Registration - Methods



- Thin-plate spline
- B-Splines
- Affine
- Diffusion
- Finite element
- ……

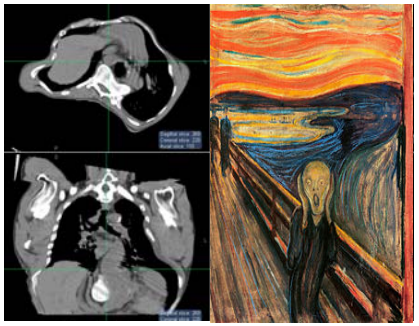


- Cross Correlation
- Mutual Information
- ……

Arts courtesy of Junyi Xia, PhD

Lack of Biomechanical Modelling

- Current software does not have a realistic modelling of the biomechanical properties of human body.



Slide courtesy of Yusung Kim, PhD

DIR: An Improving Technology

- More realistic methods are coming up.
- Example: rigid bones; flexible joints.

Clinical Application at UIHC

- An ongoing learning process
- Timeline:
  - Jun 2012: Installation, acceptance, and training.
  - July–Oct. 2012: Commissioning (*It was a struggle!*)
  - Oct. 2012: Ready for clinical use.
  - December 2012: Dose mapping commissioned.
  - Jan 2013: Ready for clinical use with dose mapping.
- Case statistics:
  - 26 documented between since 3/2013; actual number may be near 40.
  - **23 of the 26 are dose mapping**.

Commissioning at UIHC

- Accuracy:
  - What is the ground truth to compare to, *if there is any*?
  - Phantom or patient: boundary of visible structures, e.g., vertebral bodies
- Precision: Inter-user consistency
- Dose mapping through CT → CT registration

Commissioning : Spatial Accuracy

- At spherical phantom surface:
  - Mean error < 0.1mm; Std. Dev. = 0.4mm
- At boundary of anatomical structures:
  - Mean error = 1.0mm, StdDev. = 0.6mm, conformity index = 0.97 (±0.1)
- Are these numbers good enough?
  - Compare to: Kirby *et al*, 2013 Med Phys 40(1) 011702:

    Evaluated a number of DIR algorithms. **Velocity yields smallest spatial error** (pelvis phantom; 95% voxels have < 5mm error).

TG-132 Recommendations

Validation Tests and Frequencies

Frequency	Quality Metric	Tolerance
Acceptance and Commissioning	System end-to-end tests	Accurate
Annual or Upon Upgrade	Data Transfer (including orientation, image size, and data integrity) Using physics phantom	
	Rigid Registration Accuracy (Digital Phantoms, subset)	Baseline, See details in Table Z
	Deformable Registration Accuracy (Digital Phantoms, subset)	Baseline, see details in Table Z
	Example patient case verification ((including orientation, image size, and data integrity) Using real clinical case	Baseline, see details in Table Z

Brock *et al*, 2013 AAPM Annual Meeting

TG-132 Recommendations

Validation Tests and Frequencies

Frequency	Quality Metric	Tolerance
Each Patient	Data transfer	Accurate
	Patient orientation	Image Data matches specified orientation (Superior/Inferior, Anterior/Posterior, Left/Right)
	Image size	Qualitative – no observable distortions, correct aspect ratio
	Data Integrity and Import	User defined per TG53 recommendations
	Contour propagation	Visual confirmation that visible boundaries are within 1-2 voxels of contours; documentation of conformity and confidence
	Rigid registration accuracy	At Planning: confirmation that visible, relevant boundaries are within 1-2 voxels; additional error should feed into margins At Tx: confirmation that visible boundaries are within PTV/PRV margins (doesn't account for intrafraction motion)
	Deformable registration accuracy	At Planning: confirmation that visible, relevant boundaries and features are within 1-2 voxels; additional error should feed into margins At Tx: confirmation that visible boundaries are within PTV/PRV margins (doesn't account for intrafraction motion)

Brock *et al*, 2013 AAPM Annual Meeting

Commissioning: User Consistency

- If absolute accuracy is difficult to gauge, consistency may be more important:

User variations based on contour mapping for all body sites.
Site-specific numbers vary.
Sensitive to exact workflow.

For all sites	Hausdorff Distance (mm)		DICE coefficient	
	Rigid	Deformable	Rigid	Deformable
Mean	1.15	0.66	0.70	0.77
Std. Dev.	1.75	0.62	0.27	0.16

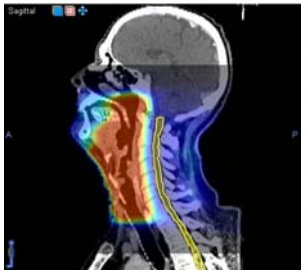
Compare to: Mencarelli et al, 2012 Med Phys 39(11) 6879-6884:
No specific algorithm or software were validated, but suggest **StdDev = 3 mm for user variance**.

Commissioning: Dose Mapping

- Dose mapping through CT→CT deformable registration:
  - CI > 0.98 and Hausdorff distance = 0.01mm (±0.15mm) between:
    - Map dose → Generate isodose contours
    - Generate isodose contours → map isodose contours
  - DVH for mapped contour and dose match original.
  - Dose re-sampling and dose summation correct (<0.01% local error)
  - CT# change has little effect; negligible inverse consistency.

More on Dose Mapping

- Not much interest in adaptive planning or dose painting, so voxel-level accuracy is not crucial.
- Main interest is OAR dose tracking. Max dose to OAR usually occurs at its boundary, which can be spot checked.
- Dose summation at dose gradient region is a tedious manual work, if possible at all.
- Biological uncertainty is far bigger and subject to physician's decision.



"Rule of Thumb" Uncertainties

Error in 95% of voxels should be below these value.

	High Contrast Region	Low Contrast Re
Brain, head & neck	3 mm	6 mm
Trunk and extremities	5 mm	7 mm
On Spine	No more than 2mm	

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UIHC Commissioning Summary & Recommendation (10/2012)

DIR Application Site	CT → CT (including PET->CT and Dose Mapping)	MR → CT
Brain, H&N, thoracic, breast, along vertebral bodies:	OK to use with validation on organ boundaries.	Possible to use with extreme caution
Liver, adrenal glands	Use with caution.	Possible to use with extreme caution
Pancreas; pelvis	Discouraged	Discouraged
Overall:	**Good in high contrast region**	**Poor performance at current algorithm**

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What really happened since then

DIR Applications	Clinical Interest	Reason
Contour mapping through CT → CT registration	Rarely	Does not save much time on review and manual editing.
MR → CT	No longer interested	Too much unrealistic deformation
PET/CT → CT	No longer interested	Better SUV2.5 location but no impact on target definition
Dose mapping through CT → CT registration.	Established clinical practice	Accurate on organ boundary; has validation methods. No alternatives in transferring dose between CT datasets.

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UIHC Workflows

Before:

1. A Velocity on-call physicist (VOP) is scheduled each week.
2. Physician determines if Velocity work is needed for a certain case.
3. If Velocity work is necessary, dosimetrist requests physicist to perform the work.

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UIHC Workflows

Physicist follows site-specific registration procedure:

Including strict naming convention and ROI selection, to minimize user variations and avoid error.

UIHC Workflows

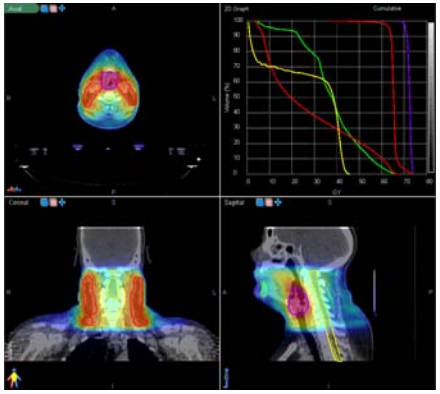
After:

1. Physician reviews the deformable registration and dose mapping with physicist and dosimetrist.
2. If approved, physicist exports deformed image dataset and/or isodose contours back to TPS.
3. Physician decides if plan is OK or needs modification.
4. Physicist documents the case.

Dose Mapping Example – Head & Neck Retreatment

Previously in Spring 2010:

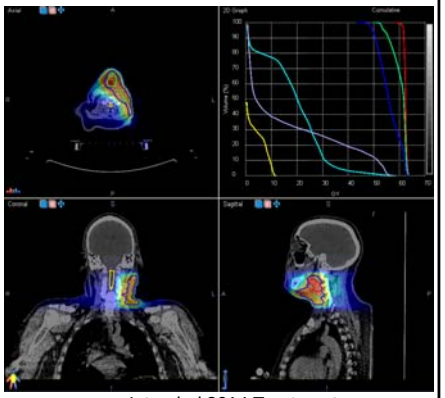
70Gy to larynx and 63Gy to bilateral necks in 35 fx IMRT.



2010 Treatment

H&N Dose Mapping Example

- Spring 2014: New mass on left neck surgically removed.
- Intention: treat the area to 45.6Gy, with boost to post-op bed up to 60Gy.
- How much total dose will the critical organs receive without the boost? Can the patient tolerate the full boost?



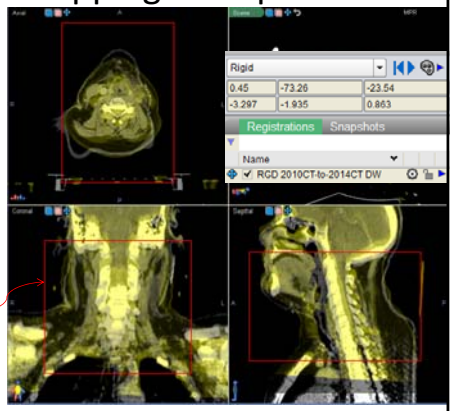
Intended 2014 Treatment

H&N Dose Mapping Example

- Step 1. Near the end of the 45.6Gy initial treatment and with the 14.4Gy boost plan ready, physician instructs dosimetrist to obtain a composite dose with 2010 dose included.
- Step 2. Dosimetrist requests dose mapping from an on-call Velocity physicist.
- Step 3. Physicist exports the following into Velocity.
  - 2010 CT + 2010 Contours, 2010 Dose
  - 2014 CT + 2014 Contours, 2014 Initial Dose, 2014 Boost Dose

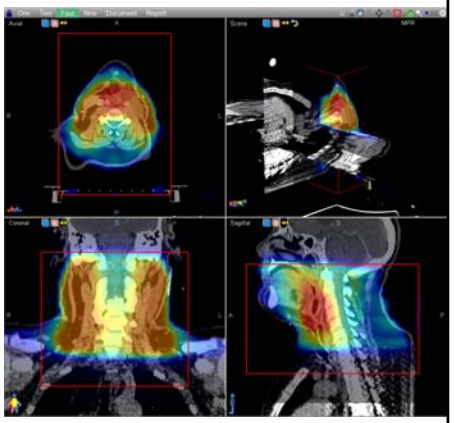
H&N Dose Mapping Example

- Step 4. In VelocityAI, physicist inspects the 2010 CT, 2010 Dose and 2014 PTVs, to find out the potential dose overlapping area.
- Step 5. Physicist performs initial rigid registration, with ROI focused on the above area.



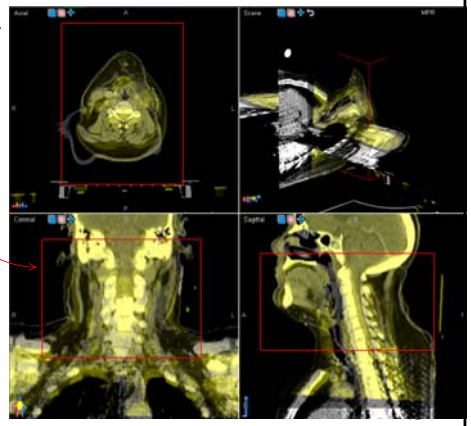
H&N Dose Mapping Example

- Step 6. Using the initial 2010CT→2014CT rigid registration, map 2010Dose onto 2014CT. Inspect and adjust the ROI.



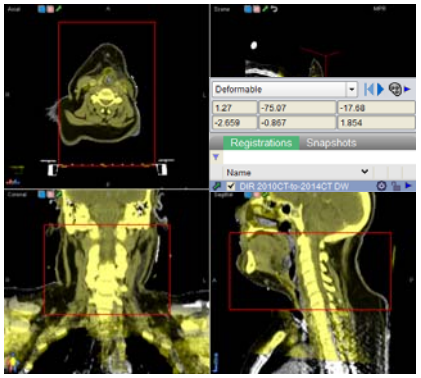
H&N Dose Mapping Example

- Step 7. Perform further 2010CT→2014CT rigid registration using the new ROI box.



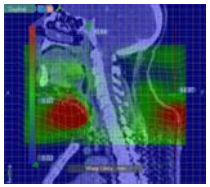
H&N Dose Mapping Example

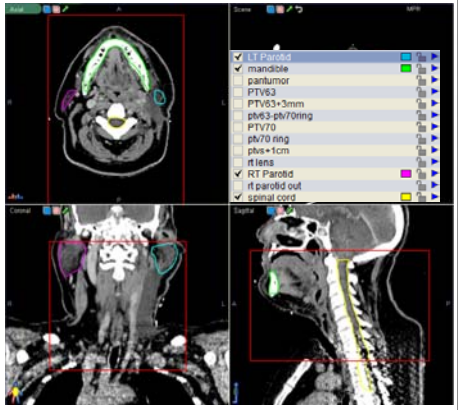
- Step 8. Based on the previous rigid registration, create and perform a deformable registration using the same ROI box.
- Step 8b (Optional). The ROI box can be further shrunk if there is a region of concern.



H&N Dose Mapping Example

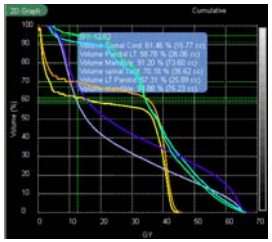
- Step 9. Check contour mapping. Examine the warp map as well.
- Possible error: "cord compression" – Velocity may compress two vertebral bodies into one when image quality is low. Check carefully.





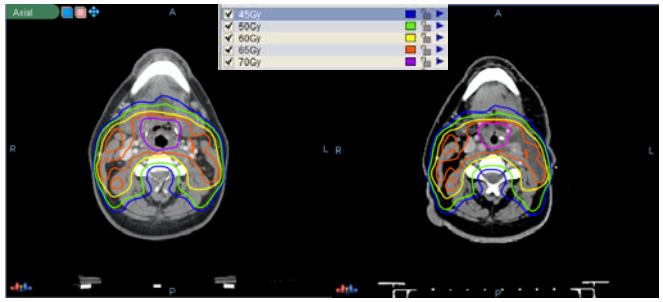
H&N Dose Mapping Example

- Step 10. Based on the previous deformable registration, map 2010Dose onto 2014CT.



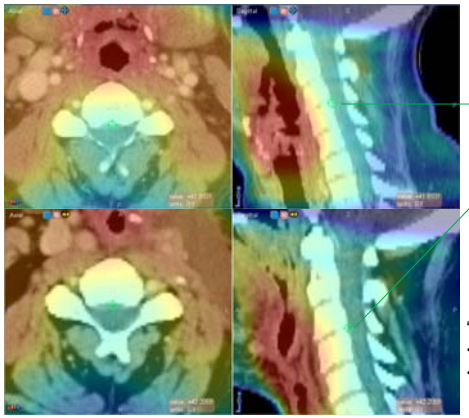
- Step 11. **Validation**:
  - Visually check mapped isodose contour distribution relative to anatomical structures.
  - Spot check point dose.
  - Compare DVH from 2010Dose+*2014 Contours* to the original DVH*(contours are often different).

Isodose Contour Check



2010 isodose lines on 2010CT 2010 isodose lines on 2014CT

Spinal Cord Dose Spot Check



2010Dose on original 2010CT: 41.9 Gy

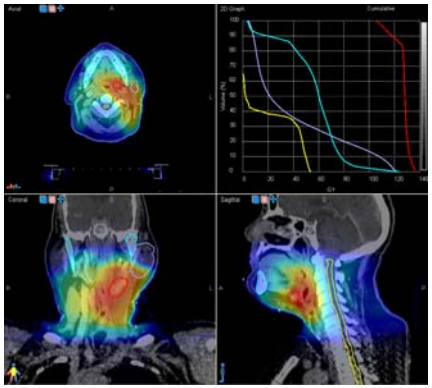
2010 Dose on 2014CT through DIR: 42.2 Gy

0.3Gy or 0.7% difference

"Rule of thumb" on spinal cord: <2 mm spatial error and <2% dose error (IMRT)

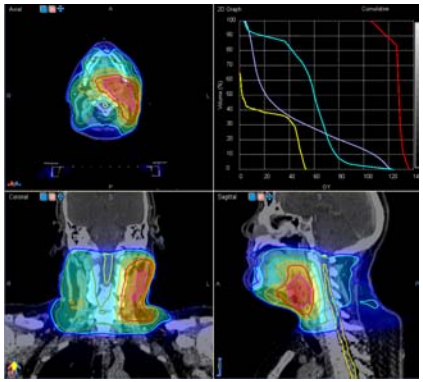
H&N Dose Mapping Example

- Step 11. Resample 2010Dose into 2014CT's FoR through DIR.
- Step 12. Sum the 2010Dose with the planned 2014Doses.
  - 2010Dose + 2014 Initial Dose
  - 2010Dose + 2014 Initial Dose + 2014 Boost Dose
- Step 13. Validate the summed maximum dose.



H&N Dose Mapping Example

- Step 14. Physician reviews the full composite dose as well as total dose up to date, decides to proceed with the full boost.
- Step 15. Physicist sends the composite isodose contours back to TPS, and documents the case.



Dose Mapping Has Clinical Impact

- Of the 23 dose mapping cases:

Clinical Decision	# of cases
Designed fields, or used previous isodose contours as avoidance structure in planning	6
Modified target volume, or changed fx number or fx schedule.	4
Sum	10 (43.5% of the total)

Summary on Deformable Registration

- Clinical deformable image registration software should be commissioned; TG-132 Report will be a good resource.
- Consistent workflow is important in reducing user variations.
- Manually validate each case by landmarks or contours.
- Make sure physicians know the uncertainties.
- UIHC clinically uses dose mapping with careful patient-specific validation.
- *VelocityAI is also a good tool for image management, even without deformable registration.*

Reflections

- By physicians:

Don't burn the bridge behind you so that we may someday *retreat*!

- By physicists:

Clinical context triumphs physics technicalities.

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