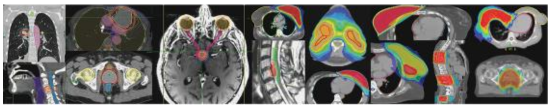
PRECISION MATTERS



Automation utilizing Deformable Image Registration in Radiation Therapy Applications

Colin Sims, M.Sc.

Overview of Deformable Image Registration (DIR)

Algorithms that can deform one dataset to another have many uses

- Manual segmentation of targets and OARS on one modality may be transformed to CT for treatment planning/ dose calculation purposes
- Autosegmentation of anatomy where atlases in one or more modalities need to be transformed to a particular patient. **Important for anatomy that cannot be easily visualized e.g. functional areas of the brain**
- In Adaptive monitoring and replanning (offline or “real-time”). Review of the dose received by the patient throughout treatment may reveal discrepancies between the planned dose and that received
- In retreatment scenarios where prior dose has been delivered and the impact of additional treatments is desired to be reviewed

Algorithm Considerations

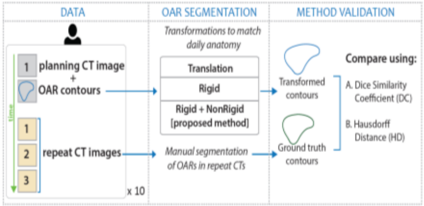
- The Accuray DIR algorithm is a proprietary non-parametric non-rigid image registration method. It assumes no specific parameterization of the transformation; instead it explicitly estimates the deformation field subject to smoothness regularization. Such an approach allows estimating even complex organ deformations. The algorithm optimizes similarity criterion, local Normalized Correlation Coefficient, which allows for robust image matching even in presence of intensity inhomogeneity and artifacts
    - It is implemented on GPU hardware and takes about 20-30 seconds to register two 3D volumes of size 512x512x300
- The algorithm uses coarse-to-fine strategy by subsequently registering 3D images at divergent hierarchical levels

Smoothing for DIR

- ***High Smoothing*** enforces the transformation to be more smooth (that is, more rigid) by sacrificing some image fidelity, which is advantageous when images are of low resolution or noisy. Multimodal registration (e.g. CT to MR) may require higher smoothness due to significant difference in intensity between the images.
- ***Low Smoothing*** allows for more flexible/local deformations by enforcing lower overall smoothness, this leads to better deformation field fidelity (especially when images are of higher quality with little noise), e.g. high-res CT-CT (4D) (or MR-MR) mono-modal registration often can benefit from Low smoothing option.
- ***Medium Smoothing*** represents a balance between deformation field fidelity and transformation smoothness.

Validation - External

Abdominal CT/CT registration evaluation workflow



Gupta, V., Wang, Y., Romero, A., Myronenko, A., Jordan, P., Heijmen, B. and Hoogeman, M. (2014), SU-E-J-208: Fast and Accurate Auto-Segmentation of Abdominal Organs at Risk for Online Adaptive Radiotherapy. Med. Phys., 41: 205. doi:10.1118/1.4888261

Validation - External

CT/CT DIR

- OARs were manually contoured by an expert panel to obtain ground truth contours for repeat CT scans (3 per patient) of 10 patients
- … we compared the propagated and ground truth contours using Dice coefficient (Dc) and Hausdorff distance (Hd). The method was benchmarked against translation and rigid alignment based auto-segmentation.
- …the auto-segmentation performed better than the baseline (translation) with an average processing time of 15 s per fraction CT
- The overall improvements ranged from 2% (heart) to 32% (pancreas) in Dc, and 27% (heart) to 62% (spinal cord) in Hd.
- For liver, kidneys, gall bladder, stomach, spinal cord and heart, Dc above 0.85 was achieved.
- Duodenum and pancreas were the most challenging with both showing relatively larger spreads and medians of 0.79 and 2.1 mm for Dc and Hd, respectively.

Validation - Internal

Three separate validation activities

- **Abdominal MR to CT deformable registration** study was conducted to evaluate the accuracy of liver multi-modal fusion when used for contouring of tumors and organs at risk on secondary MR images
  - Ground truth liver surface contours defined on a CT image were compared to deformed contours delineated independently on the secondary MR image.
- **Lung CT to CT registration study** was conducted to quantify mono-modal registration accuracy on manually annotated 4D CT datasets
  - Ground truth lung key points, manually placed at distinct anatomical locations such as vessel and airway bifurcations, were compared between end-exhale and deformed end-inhale CT images
- **kVCT to MVCT registration study** – unpublished worked based on data obtained from Accuray collaboration sites

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Validation - Internal

CT/MR DIR (unpublished)

- Liver surface misalignment error and liver fiducial misalignment error were used to evaluate the DIR algorithm in abdominal CT/MR applications.
- Liver surface was contoured on CT and MR images independently and subsequently compared after deformable registration. Two error measures were used
  - Mean 3D surface distance
  - DICE coefficient.
- An average Hausdorff distance was computed, that is for each sample point of one 3D surface we find the closest point in the other 3D surface, which produce a set of point-wise distances. The average point-wise surface distance and the maximum distance/error were computed

Liver surface misalignment for different deformable fusion options:

	Rigid (mm)			Medium Smoothing - Default (mm)			High Smoothing (mm)			Low Smoothing (mm)		
Case	Mean	95pct	Max	Mean	95pct	Max	Mean	95pct	Max	Mean	95pct	Max
Case 1	1.93	4.25	7.94	1.05	2.47	7.35	1.08	2.55	8.61	1.21	3.24	9.00
Case 2	1.76	4.90	7.53	1.14	2.57	5.12	1.13	2.52	5.10	1.23	2.81	7.13
Case 3	1.56	4.04	10.18	1.37	3.2	7.02	1.35	3.11	7.04	1.34	3.04	7.05
Case 4	1.74	4.38	12.87	1.41	3.38	11.60	1.43	3.35	11.86	1.49	3.60	11.66
Case 5	2.01	5.55	8.93	1.51	3.60	8.08	1.49	3.48	7.53	1.69	4.30	8.77
Case 6	2.36	5.55	10.29	1.48	3.45	8.86	1.49	3.54	7.74	1.57	3.84	9.32
Case 7	1.50	3.89	9.73	1.35	3.05	6.74	1.32	2.97	6.90	1.72	4.77	9.21
Case 8	1.72	4.99	11.91	1.54	3.55	13.54	1.45	3.26	11.83	2.60	8.42	13.19
Case 9	1.71	4.06	7.74	1.42	3.43	6.63	1.42	3.33	6.47	1.43	3.54	6.49
Case 10	1.99	5.13	7.55	1.27	3.08	8.87	1.31	3.29	9.12	1.50	3.83	10.66
MEAN	**1.82**	4.67	9.47	**1.35**	3.17	8.38	**1.35**	3.14	8.22	**1.57**	4.14	9.25

Validation – Internal/External

CT/MVCT DIR (unpublished)

- Contours were transferred from a planning CT image to an MVCT image and modified manually to create the 'truth' MVCT contours
- Then a deformable registration (after initial rigid) is computed between the planning image and MVCT using DIR
- The deformed planning contours are transferred to the MVCT and compared against the 'truth' MVCT contours
- Contours considered" Parotids, Optic Tree, Mandible, Canal

Average surface distance in mm of 15 cases from two institutions: average of ~8 fractions per case:

	Left Parotid (mm)	Right Parotid (mm)	Brainstem (mm)	Left Globe (mm)	Right Globe (mm)	Left Lens (mm)	Right Lens (mm)	Left Nerve (mm)	Right Nerve (mm)	Larynx (mm)	Mandible (mm)	Chiasm (mm)	Canal (mm)
Average	1.88	1.72	3.32	1.67	1.84	1.96	1.26	1.0848	1.55	1.76	1.25	1.18	3.03
SD	0.78	0.68	0.93	1.33	1.43	0.87	0.53	0.45	0.60	0.97	1.40	0.62	3.66

DIR QA

Methods Available

- Direct visualization of the vectors field. Arrows show magnitude and direction of the deformation vectors
- Warped grid showing displacement of voxels relative to the original image
- Overlay of the deformed image on the original with tools similar to those used for rigid registration
  - Objection is that the result will nearly always look good but the display doesn't demonstrate local variation in deformation, especially discontinuities or sharp changes
- DICE or other similarity metrics applied to objects deformed through the DVF
- Jacobian determinant transformation map indicating local change in volume when registering one image to another
- RegReveal© tool
  - A small sampling cube is used to determine a local *rigid* registration that approximates the local deformable registration
  - The local rigid registration is applied within a large sampling cube box to illustrate magnitude and direction of the rigid registration
  - As you move the cross hair, the local rigid registration is updated in real time
- Use of phantoms/ independent software e.g. IMSIM QA

Direct visualization of deformation in liver case

Not Registered

Direct visualization of deformation in liver case

Rigid Registration to Planning CT

Rigid image registration finished

Direct visualization of deformation in liver case

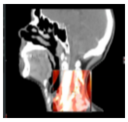
Deformable Registration to Planning CT

Other QA Tools

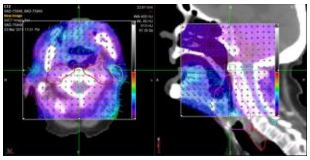
Vector Maps and MIM's Reg Reveal©

RegReveal

- A local rigid registration is computed to approximate the deformation in a small sampling box
- This rigid transformation is then applied outside the sampling box
- As one make small adjustments in the crosshair position, shifts/rotations outside the center sampling box should be reasonably stable in the absence of discontinuous changes in the vector field
  - Large fluctuations may imply a deformation that is not physically realistic

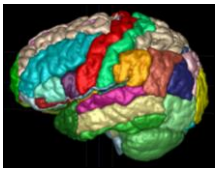


DIR Vector Maps

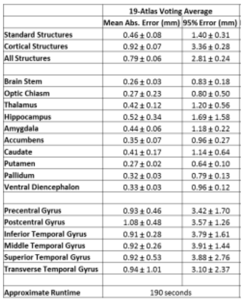


Brain AutoSegmentation

- Deformation algorithm
  - Higher segmentation accuracy
  - Fast implementation on GPU enables use of many atlases (~30 seconds for typical SRS imaging series)
- 50 neuro-anatomically labeled MRI scans
  - 50 adults (19 - 95 years old)
  - Additional 13 pediatric cases (5 – 16 years old) for testing purposes
- 157 structures per brain atlas with cortical parcellations
- Adheres to BrainCOLOR labeling protocol



Autosegmentation Accuracy



	19-Atlas Voting Average	
	Mean Abs. Error (mm)	95% Error (mm)
Standard Structures	0.46 ± 0.08	1.40 ± 0.31
Cortical Structures	0.92 ± 0.07	3.36 ± 0.28
All Structures	0.79 ± 0.06	2.81 ± 0.24
Brain Stem	0.26 ± 0.03	0.83 ± 0.18
Optic Chiasm	0.27 ± 0.23	0.80 ± 0.50
Thalamus	0.42 ± 0.12	1.20 ± 0.56
Hippocampus	0.52 ± 0.34	1.69 ± 1.58
Amygdala	0.44 ± 0.06	1.18 ± 0.22
Accumbens	0.35 ± 0.07	0.96 ± 0.27
Caudate	0.41 ± 0.17	1.14 ± 0.64
Putamen	0.27 ± 0.02	0.64 ± 0.10
Pallidum	0.32 ± 0.03	0.79 ± 0.13
Ventral Diencephalon	0.33 ± 0.03	0.96 ± 0.12
Precentral Gyrus	0.93 ± 0.46	3.42 ± 1.70
Postcentral Gyrus	1.08 ± 0.48	3.57 ± 1.26
Inferior Temporal Gyrus	0.91 ± 0.28	3.79 ± 1.61
Middle Temporal Gyrus	0.92 ± 0.26	3.91 ± 1.44
Superior Temporal Gyrus	0.92 ± 0.53	3.88 ± 2.76
Transverse Temporal Gyrus	0.94 ± 1.01	3.10 ± 2.37
Approximate Runtime	190 seconds	

Background to Adaptive Therapy

Personalized, Precision Therapy

- Patients lose weight and tumors shrink during the course of treatment, especially when the course is long (28-40 fractions)
- The delivered dose can differ significantly from what was planned
  - Too much dose to critical organs and/or too little to the tumor
- Physicians want to know when this occurs and what to do about it
- Monitoring the dose delivered during treatment is complex, time consuming and creates a lot of data
- Adaptive approaches have been around for a long time but widespread adoption appears to be very limited
- Probably most patients won’t need adaption (replanning) but you don’t know which ones they are unless you monitor them all

Adaptive Monitoring

Personalized, Precision Therapy

- Attempt to maintain the integrity of original plan
  - Ensure tumor coverage
  - Preserve OAR dose
- Enable monitoring for all patients not just a selected few
- Monitoring should be based on dose not a surrogate like weight
- Enable the user to set protocol specific action levels to flag when further investigation is warranted
- Enable efficient replanning when indicated
  - 10–30% of patients for some applications?
  - Ex: Parotid mean dose likely trigger for replan in H&N

Adaptive Monitoring - Automation and Data Handling

Adaptive therapy can **only** be accomplished through significant automation and efficient handing of the very large amount of data created.

ALL of this AUTOMATIC:

- Creates a “merged” image (daily MVCT plus registered kVCT)
- Calculates the dose on the daily image
- Deforms the planning VOIs onto the daily image
- Deforms and accumulates the daily dose on the treatment planning CT
- Daily, Accumulated and Projected plan metrics to be used in automatically created reports
- Generates user-defined reports
- Flags for review if any structure exceeds dose or dose-volume tolerances
- Archival of all data including images, contours and doses across the complete course of treatment

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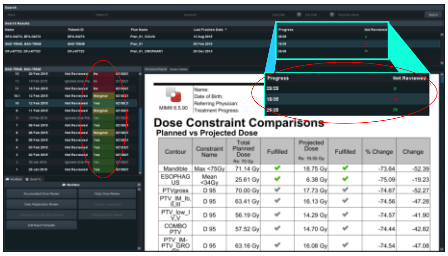
Patient Status at a Glance

Patients

Fractions



Dose Constraint Comparisons

Planned vs Projected Dose

Contour	Constraint Name	Total Planned Dose Rx: 70 Gy	Fulfilled	Projected Dose Rx: 19.55 Gy	Fulfilled	% Change	Change
Mandible	Max <75Gy	71.14 Gy	✓	18.75 Gy	✓	-73.64	-52.39
ESOPHAGUS	Mean <34Gy	25.61 Gy	✓	6.38 Gy	✓	-75.09	-19.23
PTVgross	D 95	70.00 Gy	✓	17.73 Gy	✓	-74.67	-52.27
PTV_IM_Ib,II,III	D 95	63.41 Gy	✓	16.13 Gy	✓	-74.56	-47.28
PTV_low_IV,V	D 95	56.19 Gy	✓	14.29 Gy	✓	-74.57	-41.90
COMBO PTV	D 95	57.52 Gy	✓	14.70 Gy	✓	-74.44	-42.82
PTV_IM-PTV_GRO	D 95	63.16 Gy	✓	16.08 Gy	✓	-74.54	-47.08

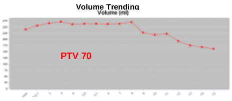
The Dashboard allows for rapid review of each enrolled patient’s treatment and status of each delivered fraction

Green = Fulfilled all user constraints
Yellow = Marginal pass
Red = Failed 1 or more constraints

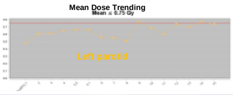
Toolkit

Automatic report with warning flags

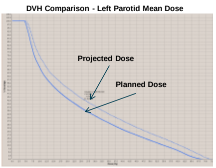
Red flags highlight dose constraints violations of the left parotid, esophagus and mandible if projected to the end of treatment



One can see a significant decrease in tumor volumes (that might have indicated the need to replan much earlier) and…

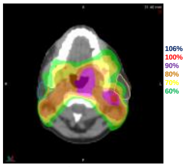


… a commensurate increase in the mean daily dose to the parotid

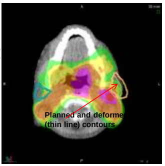


One can clearly see that mean dose to the left parotid will be significantly increased over the planned value if the dose at fraction 15 is projected out to the end of treatment..

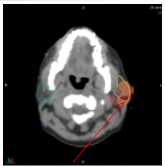
Fraction 15 Review



From treatment plan

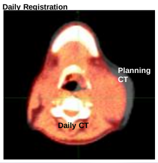


From daily CT

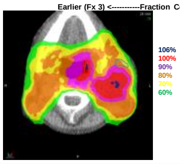


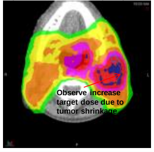
Dose Difference (parotid in high dose region)

Daily Registration



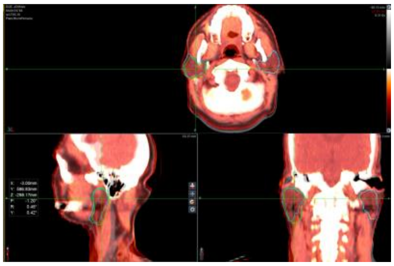
Earlier (Fx 3) <-----------Fraction Comparison-----------→ Later (Fx 15)





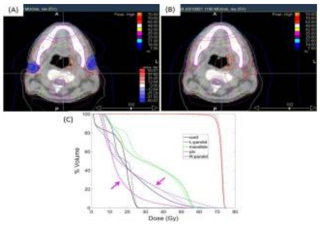
Deformable v Rigid Registration

- Some don't trust deformable operations and would prefer or like to see a rigid transform, at least for comparison



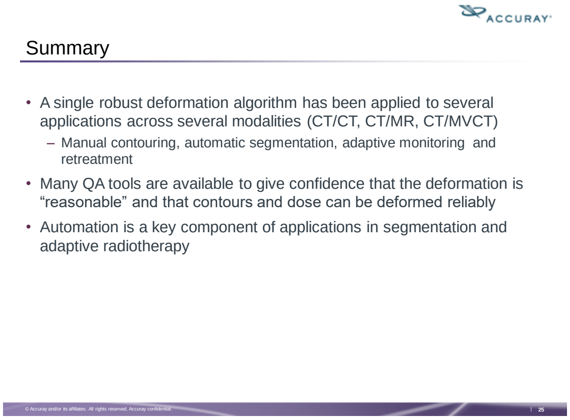
- The blue contours are the original parotids rigidly transformed to a new planning CT series
- The greens are the deformed parotids
- The red overlay is a new CT scan overlaid on an older one

Replanning example



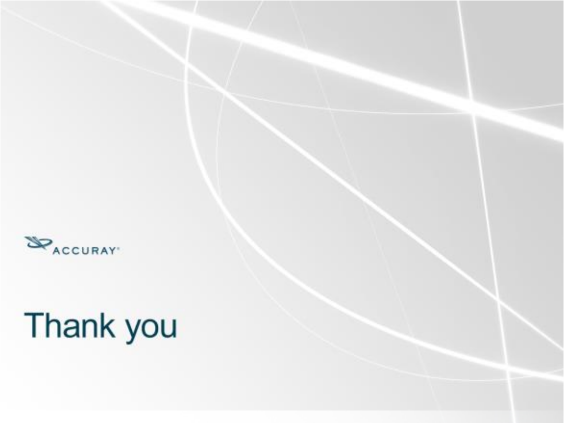
Isodose distributions for (**A) an adaptive re-plan** of the head-and-neck case, from analysis of fraction 13, and **(B) the non-adaptive re-plan** of the case that would have been created and delivered clinically for the patient after fraction 25. **Regions of reduced dose within the adaptive re-plan relative to the clinical re-plan are indicated as blue color-wash in (A).** Shown in (C) are the DVH distributions for the adaptive re-plan (solid lines) and for the non-adaptive re-plan (dashed lines); arrows indicate the DVHs for the right parotid.

Data courtesy Froedert Hospital, Medical College of Wisconsin



Summary

- A single robust deformation algorithm has been applied to several applications across several modalities (CT/CT, CT/MR, CT/MVCT)
  - Manual contouring, automatic segmentation, adaptive monitoring and retreatment
- Many QA tools are available to give confidence that the deformation is "reasonable" and that contours and dose can be deformed reliably
- Automation is a key component of applications in segmentation and adaptive radiotherapy



Thank you