Longitudinal Imaging in Radiation Therapy

John M. Buatti, MD
Professor and Chair Dept. Of Radiation Oncology
University of Iowa Carver College of Medicine

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Conflict of interest

Editor: Up to Date

Quantitative Imaging

Quantitative imaging is the extraction of quantifiable (measurable) features from medical images for the assessment of normal or the severity, degree of change, or status of a disease, injury, or chronic condition relative to normal

- **Treatment planning**
- **Prediction of outcome**
- **Measurement of progression**

The Goal: Create the condition where all imaging scanners perform as measuring instruments.

QIN Mission Statement

“The mission of the Quantitative Imaging Network (QIN) is to improve the role of quantitative imaging for clinical decision making in oncology by the development and validation of data acquisition and analysis methods as applied to prediction and response to drug or radiation therapy.”

The QIN Enterprise

35 teams have participated
Currently: 17

Pipeline for QI Tool Development

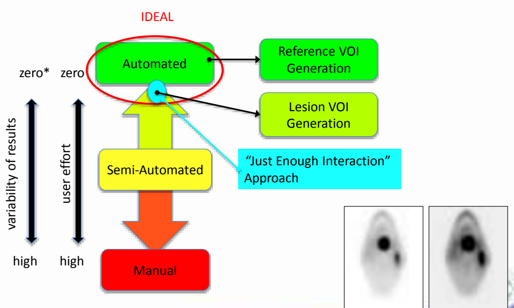
Image Analysis Output

1. Volume of interest (VOI) masks for structures with uptake:
   - Reference regions (similar to PERCIST[+])
   - Primary cancer
   - Lymph nodes
2. Quantitative indices derived from segmented VOIs:
   - SUVmax, SUVpeak, SUVaverage, Volume, Metabolic Tumor Volume (MTV), …
   - Indices may also be based on CT data

[+] *R.Wahl et al. From RECIST to PERCIST: Evolving Considerations for PET response criteria in solid tumors. J Nucl Med. 2009.*

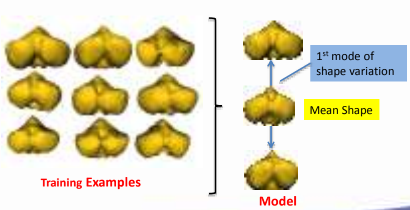
Segmentation Approach

→ key for success (usability)



Cerebellum VOI Algorithm

- Based on a **Robust Active Shape Model**
- Learn shapes of cerebella → model
- Match model to new image data → VOI



Example of a Resulting Cerebellum VOI

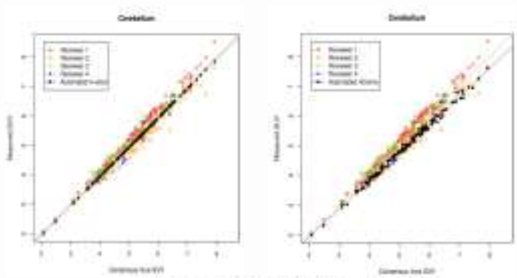
Validation – Image Data

- 134 PET/CT scans from 49 subjects with H&N cancer
- F-18 FDG (370 MBq+/-10%)
- Uptake time 90 min +/- 10%
- Subjects fasted >4h
- Blood glucose <200 mg/dl
- Arms down
- 128x128 pixel matrix (3.5 x 3.5 x 3.4 mm) or 168 × 168 pixel matrix (3.4mm × 3.4mm × 2.0mm)

Validation - Uptake in Cerebellum

- Independent reference standard:
  - Experts manually traced the cerebellum in 4 cross-sections (1 axial, 1 coronal, 2 sagittal [left & right hemisphere])
  - 2 experts: 134, 1 expert: 44, and 1 expert: 20
  - Average SUV from all 4 cross-sections
  - Consensus-true SUV model based on expert results + statistical analysis approach

Validation - Uptake in Cerebellum



[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]
	Volume	[illegible]	[illegible]

(95% credible intervals)

Comparison Automated vs. Manual

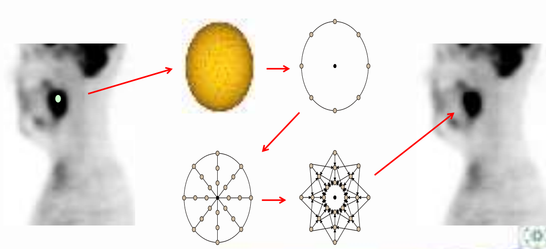
Decrease in total variability if the automated method was used instead of the manual method:

Cerebellum	4-Slice	99.2% *
	Volume	89.8% *
Aortic arch	Volume	76.7% *
Liver	Volume	54.7%

** … statistically significant*

VOI Generation for Lesions

- Segmentation problem → graph-based optimization approach (Optimal Surface Segmentation)
- Graph + cost function (design is critical!)
- Integrated into 3D Slicer (www.slicer.org)



Complexity issues

Complexity issues

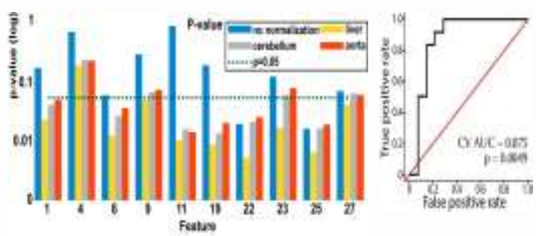
Generating Data

- SUV Max, Mean
- Metabolic Tumor Volume
- Range Pixel Values
- Volume over/x SUV
- Normalization against
- Liver/Blood Flow
- Lowest Quartile
- Highest Quartile
- Etc…………..

PET Module Tool – publicly available

https://slicer.org

Types of Analyses



Validation Study

- Using a set of 60 cases with 230 lesions
  - 3 investigators randomly contoured each case using manual (twice) or PET module tool (twice)
  - 2760 contoured lesions
  - Compared for internal consistency and against best estimate of ground truth

Automated tool agreement

Table 1

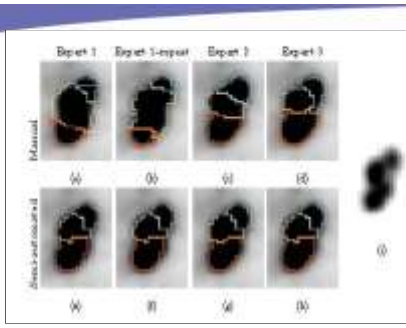
		Manual		Semi-automated	
Agreement	N	Mean	95% CI	Mean	95% CI
Within Operator	600	77.3	(74.7–79.4)	92.6	(90.2–94.3)
Between Operator	600	79.8	(78.4–81.2)	94.1	(92.7–95.6)

Table 1. Estimated mean dice coefficients for intra and inter-operator segmentation agreement.

Table 2

Method	Time (minutes)	95% CI (minutes)
Manual	8.88 ± 7.1	(6.47, 11.26)
Semiauto	3.74 ± 3.3	(2.40, 5.08)

Table 2. Estimated mean times with standard deviation and 95% confidence intervals (CI) for manual and semi-automated segmentations.



Example of intra- and inter-operator segmentation agreement for manual and semi-automated segmentation methods. (a-d) Manual slice-by-slice segmentation results. (e-h) Semi- automated full 3D segmentation results. (i) Same PET image as in images (a-h), but with a different gray-value transfer function, showing uptake peaks corresponding to individual lymph nodes in close proximity.

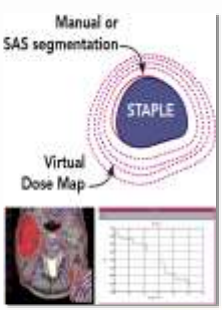
The Value Proposition for Quantitative Imaging in Oncology Trials - Specific use cases

- PET
  - SUV for lymphoma (CALGB 50303)
  - PERCIST as a response criteria (EA developing concept:EA1172)
- MRI
  - Breast cancer volume (ISPY-1/ACRIN 6657 / CALGB 150007), ADC (I-SPY2/ACRIN 6694)
  - ADC (Apparent Diffusion Coefficient) for head and neck cancers (UO1 CA211205-01)
- CT
  - Volumetric CT measures in NSCLC 80802 trial
  - Development of radiomics as a parallel to genomics in clinical trials

Representative tools developed by QIN teams

Tool	Modality	Purpose
Lymph node segmentation	MRI	Lymph node segmentation
Xcal	PET	Multicenter PET SUV cross-calibration
AutoPERCIST	PET	PERCIST response analysis for FDG-PET
Lung Segmentation	CT	Volumetric lung nodule segmentation
Radiomics analysis	CT	Lung, head and neck radiomics analysis
Mass estimation	CT	Muscle mass of cancer patients
ePAD	Image analysis	Image annotation and quantitative analysis
Slicer	Image analysis	Image analysis and surgical planning

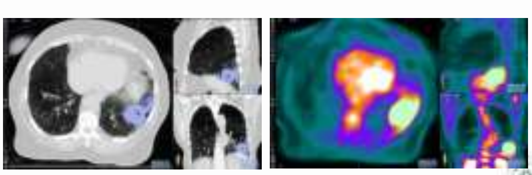
Tumor Control Probability



(Top) A virtual dose map was generated from each manual contour (Manual-C) or semi-automated segmentation (SAS). (Bottom) Its dose gradient was -2.7 % per mm, adapted from a clinical head-and-neck intensity-modulated radiation therapy (IMRT) plan.

PET-CT Co-Segmentation

- Tumor contours on PET and on CT are different
  - PET and CT may not well aligned
  - Use different imaging mechanisms



PET-CT Co-Segmentation Software

- Simultaneously segmenting both tumor contours on PET and CT
  - Mutually use the information from the other modality
    - Admit the difference between the contours.
- Implemented as a 3D-Slicer extension module with GUI

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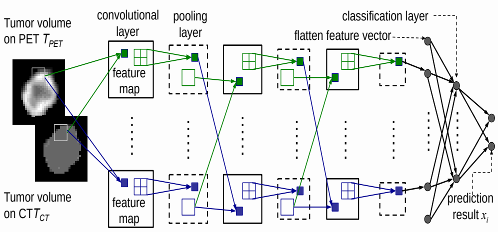
Innovation

- Deep learning for predicting therapeutic response to radiation therapy



  - Data driving
  - Automated extract highly expressive imaging features for response prediction

Conclusions

- Quantitative imaging represents an opportunity to improve both our ability to consistently improve response assessment and prognostication of cancer (and targeting).
- Algorithmic tools are critical components to leverage the big data source and will be combined (multiparametric) with both other imaging and radiogenomics.

Conclusion

- As the complexity increases, the ability of strictly simple principles that have commonly guided therapy decision making is likely to go away
- Opportunity ripe for adoption in prospective multi-institutional clinical trials in development. Validation and biomarker discovery for oncology decision making using quantitative imaging is an exciting area of investigation.

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