Image Treatment Response Assessment: How Important is Quantification?

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Isn't it obvious?

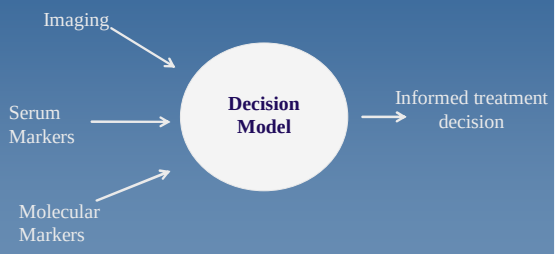
It is important

Isn't it obvious?

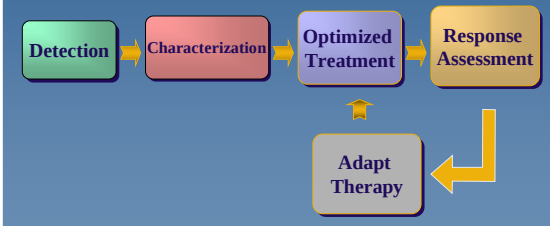
It is important

…then why do we ask the question?

Diagnostics and clinical decisions



Role of imaging in cancer care



Imaging as a system

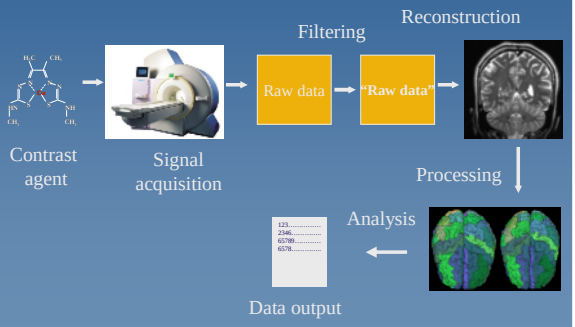
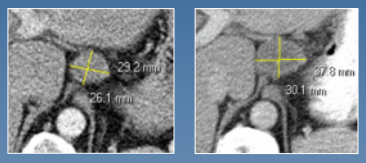


Image Data

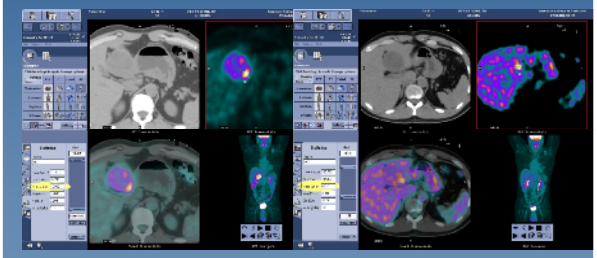
- Size
- Architecture
- Perfusion/blood flow
- Metabolism
- Diffusion
- Proliferation
- Hypoxia

RECIST Response



RECIST
LD = 2.9 cm
LD = 3.8 cm
31% increase → **PD**

GIST metabolic response: ACRIN 6665



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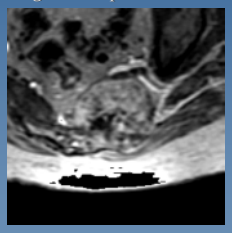
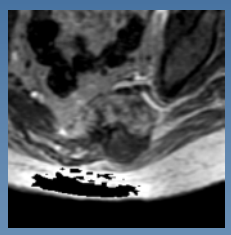
Treatment decisions for RT

Compare tumor characteristics prior to and after therapy

- Global response
- Regional response



Pre-treatment



Post-treatment

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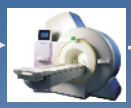
Imaging as a system

Contrast agent



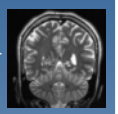
Signal acquisition

Filtering

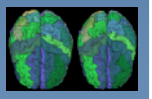
Raw data

Reconstruction

"Raw data"



Processing



Analysis

Data output

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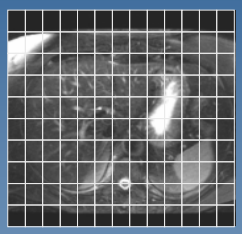
Imaging as a source of data

Feature 1
Feature 2
Feature 3
.
.
.



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Reducing the image to data

- Global assessment
  - Detection, diagnosis, time point comparison
- Categorical classification
  - Qualitative, semi-quantitative
- Human extracted quantitative data
  - RECIST, ROI based measurements
- Automated quantitative data
  - Tumor volume segmentation

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Reducing the image to data

- Global assessment
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Qualitative Imaging

- Human extracted quantitative data
  - RECIST, ROI based measurements
- Automated quantitative data
  - Tumor volume segmentation

Quantitative Imaging

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Qualitative Imaging

- Positive
  - Ease of implementation
  - Platform independent
  - Observers can control for artifacts, orientation, and technique
- Challenges
  - Dependence on presentation
  - Inter and intra observer variability
  - Limited dynamic range
  - Bias (lack of feature independence)
  - Training/credentialing challenge

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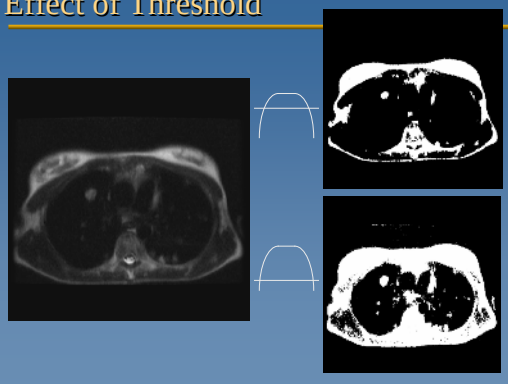
Effect of Threshold



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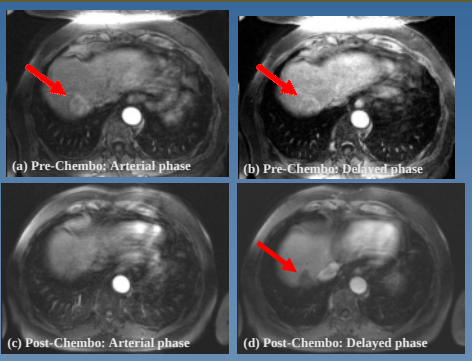
Qualitative Imaging



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Results: Reader agreement and RR vs. OS

Model	Fleiss' Kappa	RR Pred of OS?
RECIST	0.211	0.96
Unconstrained RECIST	0.238	N/A
WHO	0.225	0.94
3D	0.163	N/A
(RECIST)*(%Nec)	0.356	0.04
(Unconst RECIST)*(%Nec)	0.412	0.02
(WHO)*(%Nec)	0.521	0.12
(3D)*(%Nec)	0.457	0.02
EASL	0.296	0.71
EASL 2D	0.458	0.04

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Quantitative assessments

- Positive
  - Un-biased
  - Data, not presentation dependent
  - In principal reduces variability
  - Larger dynamic range
- Challenges
  - Generalizability across platforms/systems
    - Maintaining forward compatibility
  - Often involves observer input (introduces variability)
  - Implementation standards
  - Adoption

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Interobserver Misclassifications by Case Using RECIST and WHO Criteria for Progressive Disease (RECIST > 20%, WHO > 25%)

	Observer Pair										
Measurement Method	1, 2	1, 3	1, 4	1, 5	2, 3	2, 4	2, 5	3, 4	3, 5	4, 5	Average
Unidimensional											
Minimum RD, %	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Maximum RD, %	130.0	170.	86.67	47.50	90.91	150.0	109.0	194.1	123.5	66.67	116.91
Median RD, %	13.33	9.62	10.00	7.14	7.79	20.00	8.85	15.00	11.11	10.34	11.32
No. of misclassifications	12	8	9	7	10	16	12	12	8	7	10.1
% of cases	36.36	24.24	27.27	21.21	30.30	48.48	36.36	36.36	24.24	21.21	30.61
Bidimensional											
Minimum RD, %	0.22	0.53	0.80	0.87	0.78	0.00	0.00	0.74	0.76	5.33	1.00
Maximum RD, %	372.2	187.5	273.3	150.7	316.6	492.5	433.3	304.4	151.4	196.4	287.88
Median RD, %	17.39	13.33	23.98	14.71	15.38	30.17	17.00	24.74	21.29	27.59	20.56
No. of misclassifications	15	9	16	8	14	21	11	16	15	18	14.3
% of cases	45.45	27.27	48.48	24.24	42.42	63.64	33.33	48.48	45.45	54.55	43.33

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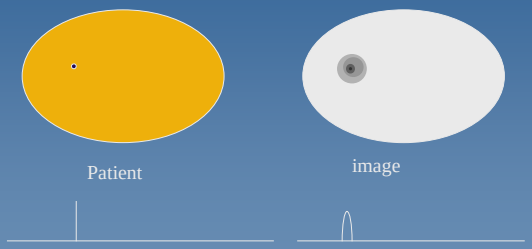
Point Spread Function



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Point Spread

- Dependent on acquisition system and reconstruction
- Effects mapping of signals onto the image
- Impacts detection of boarders
- Impacts peak signal values
- Impacts relationship of signals between modalities

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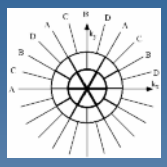
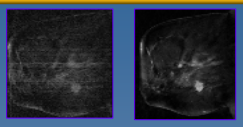
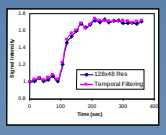
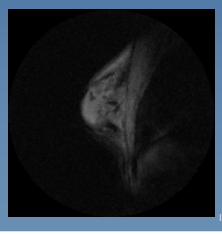
Shared signal data to accelerate reconstruction





"pure" image "time filtered" image





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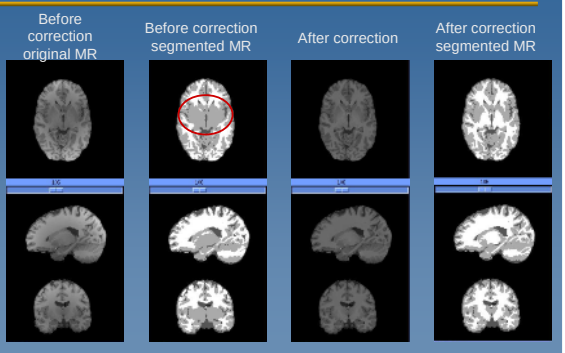
Technology Evolution: 8 Channel Array upgrade



Christos Davatzikos et al

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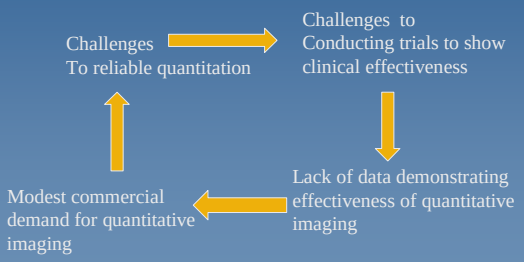
Why do we ask the question?



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What is needed?

- Extraction of (quantitative) data from images that:
  - Has dynamic range consistent with the biology
  - Is generalizable
  - Survives platform variability
  - Survives system upgrades
  - Can be implemented with minimal overhead

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