# Changes in enhancing tumour volume at MRI in response to neoadjuvant chemotherapy for primary breast cancer: correlation with pathological response

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# Background (1)

- Neoadjuvant chemotherapy (NAC) is increasingly used in primary breast cancer according to tumour biology and immunophenotype
- Ultimate pathological response predicts for disease-free and overall survival[1]

[1]*Symmans et al JCO 2007; 25:4414-4422*

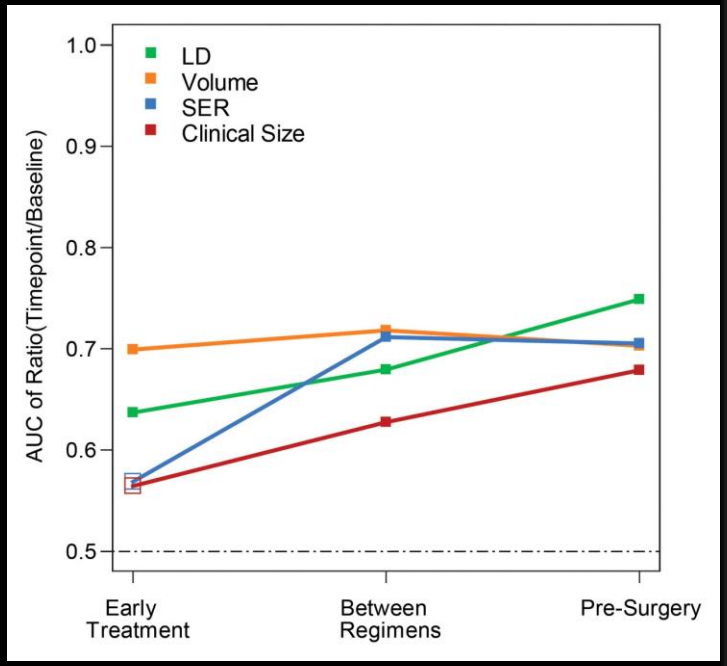
# Background (2)

- Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) is often used to monitor response to NAC

- MRI metrics that identify likely responders to NAC early on could facilitate surgical planning and enable a more personalised approach to treatment

# Background (3)

- ACRIN 6657 I-SPY 1 trial[1]:
  - Early change in functional tumour volume (FTV) best predicted pathological response
  - Volume assessment used enhancement threshold of 70%




[1]*Hylton et al Radiology 2012*

# Background (4)

- FTV utilises a fixed enhancement threshold
  - Pixels with signal intensity exceeding this threshold are included in the tumour volume
- Tumour volume could be erroneously low if slowly enhancing pixels are excluded
- User defined semi-automated thresholding techniques might be more accurate

# Aims

- To assess whether early changes in semi-automated measures of enhancing tumour volume (ETV) could predict pathological response

- To assess intra-observer and inter-observer repeatabilty of ETV measurements

# Methods (1)

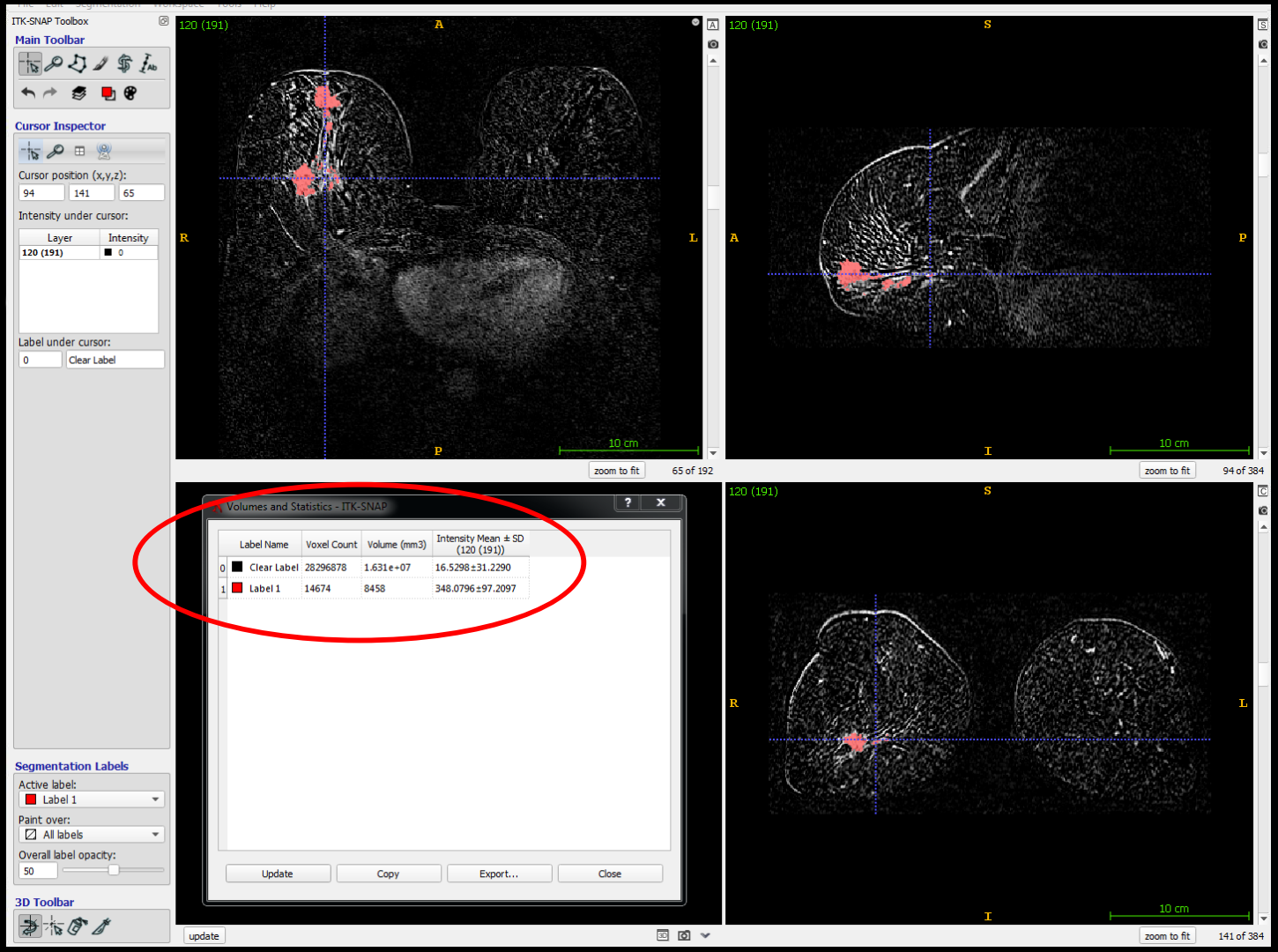
- Retrospective study of 103 consecutive patients undergoing NAC for primary breast cancer
- Informed consent waived; patients consented to use of images
- Baseline (pre-NAC) and interim (after 2 or 3 cycles) MRI on 1.5T or 3T Siemens scanner

# Methods (2)

- 2 minute post-contrast subtracted series used
- ETV was analysed offline by 1 observer using the semi-automated segmentation tool in ITK-Snap[2]
- Repeated after a minimum 1 month interval to assess intra-observer reproducibility and second observer also analysed volumes
- Measurement time 2-3 minutes

*Yushkevich et al NeuroImage. 2006;31:1116-28*

# ITK-Snap


ITK-SNAP Toolbox
Main Toolbar
Cursor Inspector
Cursor position (x,y,z):
94
141
65
Intensity under cursor:
Layer
Intensity
120 (191)
0
Label under cursor:
0
Clear Label
Segmentation Labels
Active label:
Label 1
Paint over:
All labels
Overall label opacity:
50
3D Toolbar
120 (191)
A
R
L
P
10 cm
zoom to fit
65 of 192
120 (191)
S
A
P
I
10 cm
zoom to fit
94 of 384
Volumes and Statistics - ITK-SNAP
Label Name
Voxel Count
Volume (mm3)
Intensity Mean ± SD (120 (191))
0
Clear Label
28296878
1.631e+07
16.5298±31.2290
1
Label 1
14674
8458
348.0796±97.2097
Update
Copy
Export...
Close
120 (191)
S
R
L
I
10 cm
zoom to fit
141 of 384
update

# Methods (3)

- Percentage change in ETV between baseline and interim calculated for each patient and by pathological response group

- Final pathology was assessed on surgical resections using residual cancer burden (RCB) scores

# Methods (4)

- RCB score quantifies pathological response[1]
  - defines categories of response in tumour bed and regional lymph nodes[2]
- Significant predictor of distant relapse free survival[1]
- Statistical comparison: Mann-Whitney U test

[1]*Symmans et al JCO 2007; 25:4414-4422*

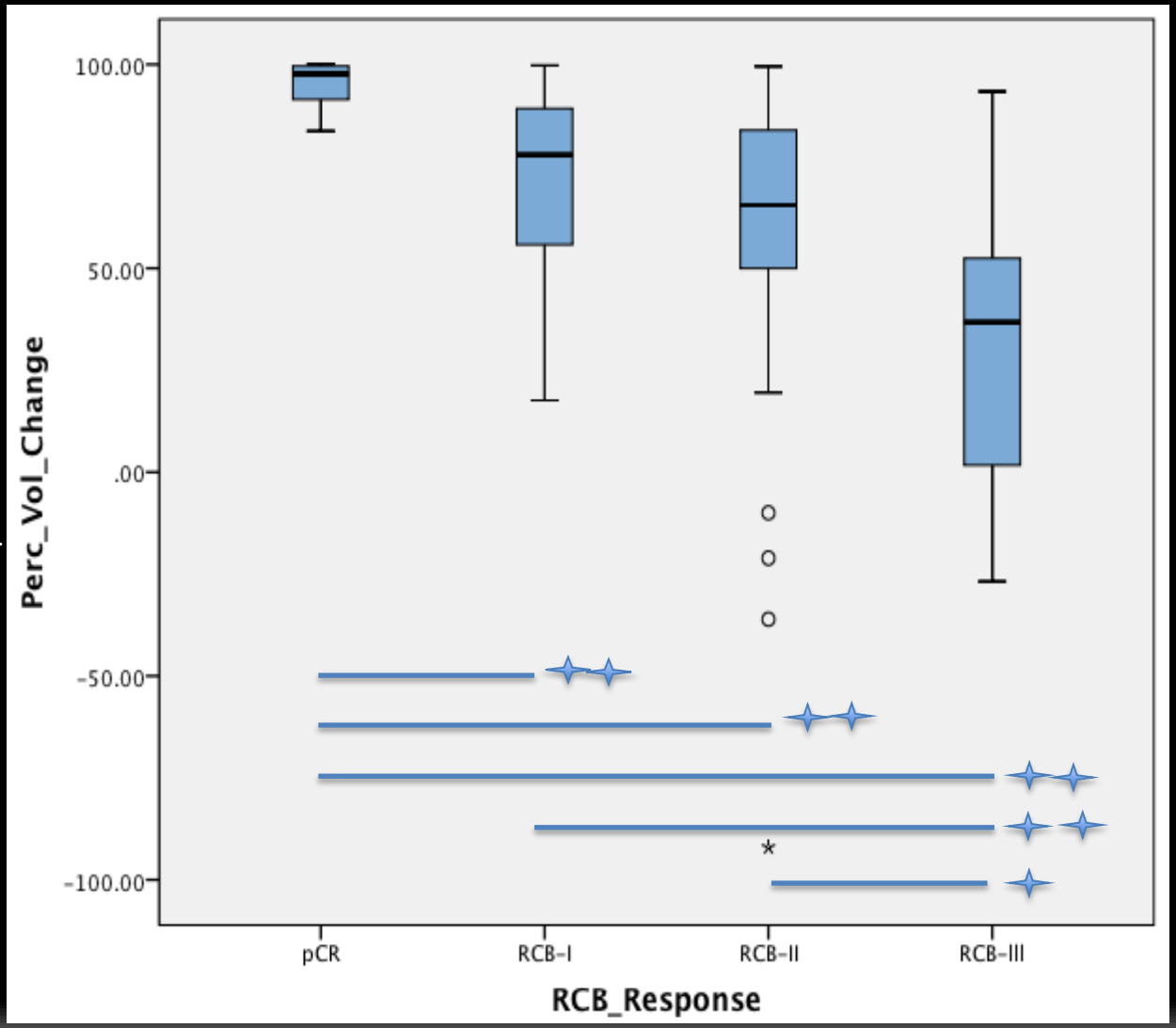
[2]*http://www3.mdanderson.org/app/medcalc/index.cfm?pagename=jsconvert3*

# Results (1)

Mean % reduction in ETV by pathological response:

- pCR *(n=18)*: 95.3% (5.4%)
- RCB-I *(n=14)*: 71.1% (23.0%)
- RCB-II *(n=51)*: 59.4% (37.3%)
- RCB-III *(n=20)*: 33.0% (34.0%)

# Results (2)



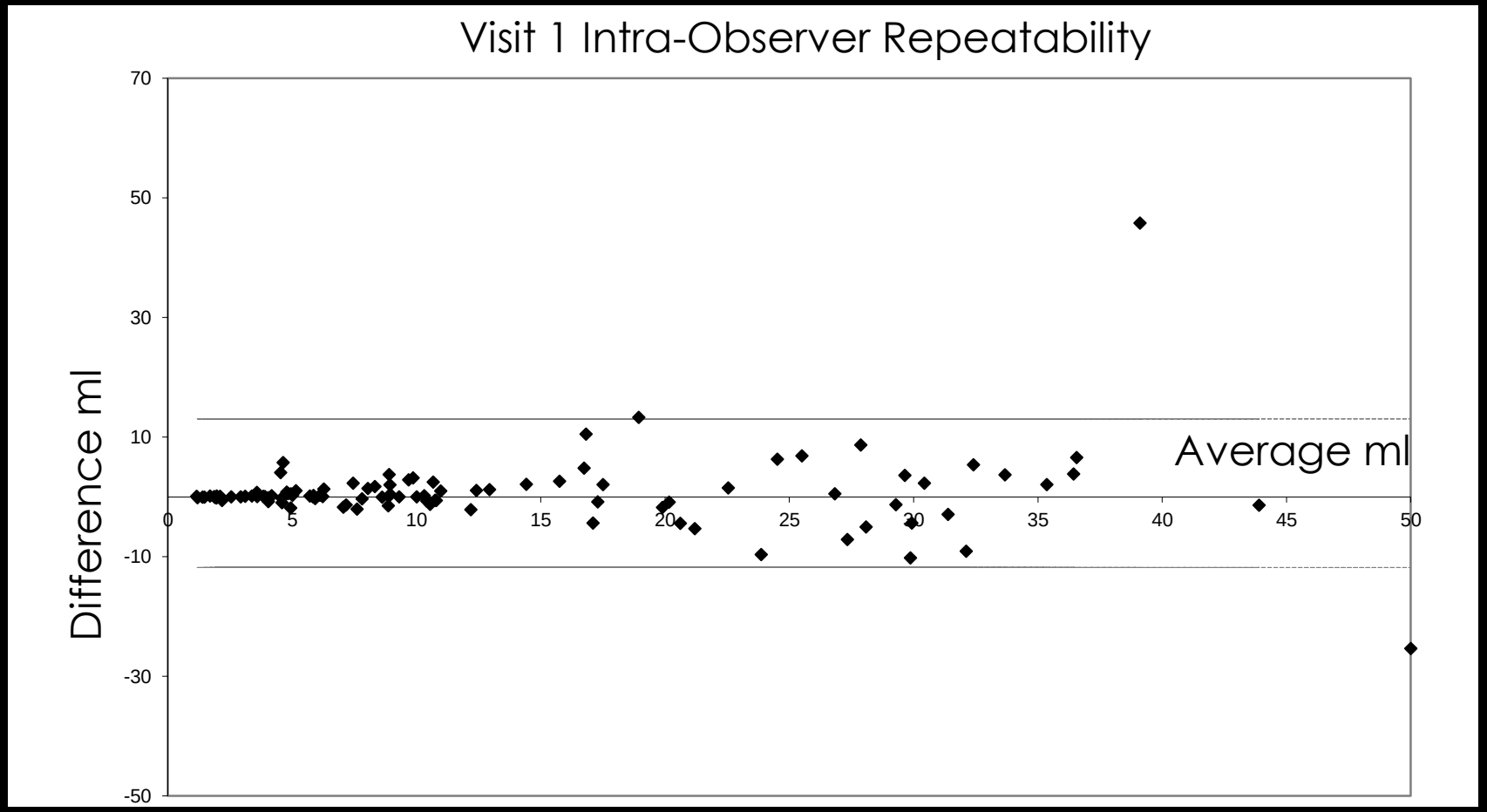

p<0.001

p 0.008

# Results (3)

| Comparison | P-value | Significant |
|---|---|---|
| Across all RCB groups | **p<0.001** | Y |
| pCR vs RCB-I | **p<0.001** | Y |
| pCR vs RCB-II | **p<0.001** | Y |
| pCR vs RCB-III | **p<0.001** | Y |
| RCB-I vs RCB-II | p=0.273 | N |
| RCB-I vs RCB-III | **p<0.001** | Y |
| RCB-II vs RCB-III | **p=0.008** | Y |

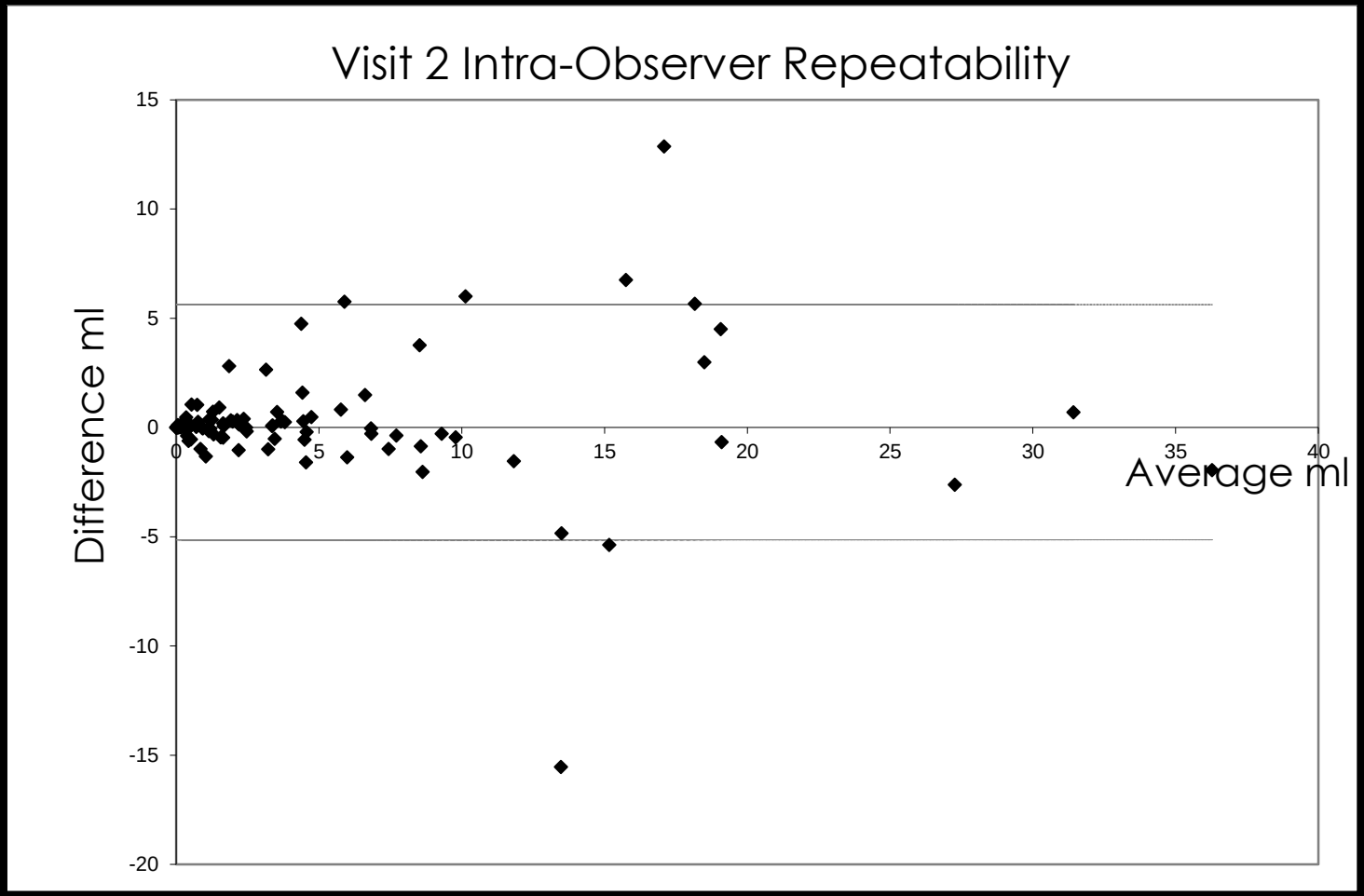
# Intra-observer repeatability of baseline ETV measurement



# Intra-observer repeatability of baseline ETV measurement

- Average ETV at baseline : 13.3 ml
- CoR : 1.5 ml
- % CoR : 11.6%

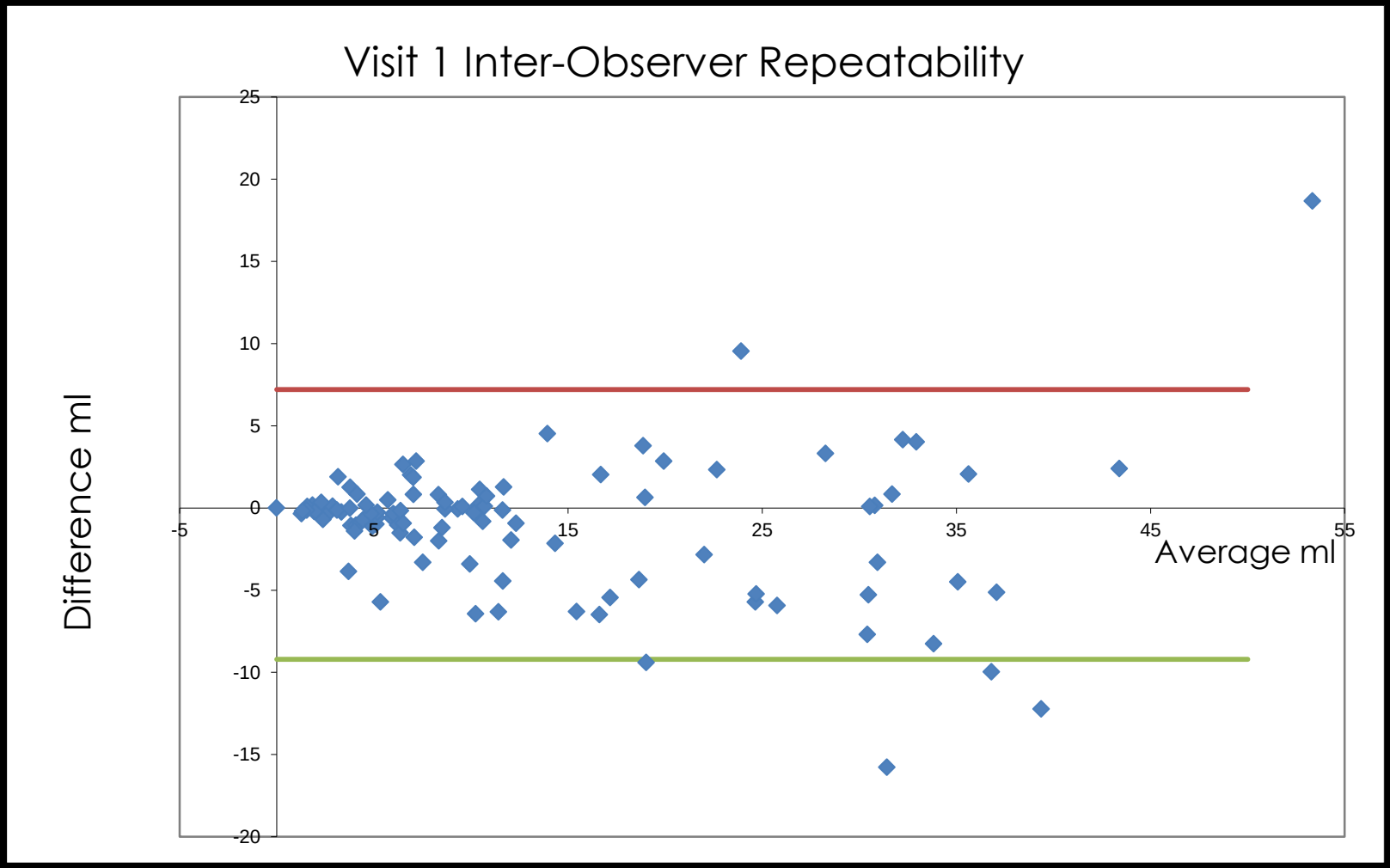
# Intra-observer repeatability of interim ETV measurement



# Intra-observer repeatability of interim ETV measurement

- Average ETV at interim : 4.8 ml
- CoR : 1ml
- % CoR : 20%

# Inter-observer repeatability of baseline ETV



# Intra-observer repeatability of baseline ETV measurement

- Average ETV at baseline: 13.3ml
- CoR : 1.9ml
- % CoR : 14.8%

# Conclusions

- Percentage change in ETV between baseline and interim MRI correlates well with pathological response to NAC using RCB score
- Good intra and inter-observer repeatability indicates that this is a potentially useful clinical tool in prediction of response

# Future Work

- Comparison of predictive ability of ETV versus fully automated FTV
- Replicate in other centres and with other softwares and vendors
- Stratify by tumour immunophenotype
- Could predictive power be shown after only 1 cycle of NAC?

# Acknowledgements

Our grateful thanks to all the patients who participated in this research

This work was partially funded by:
Breast Cancer Now
EPSRC
EU FP7