# Predicting Response to Neoadjuvant Chemotherapy using Textural Analysis

P. Gibbs[1], D. J. Manton[1], M. Lowry[1], L. W. Turnbull[1]
[1]MRI Centre, University of Hull, Hull, United Kingdom

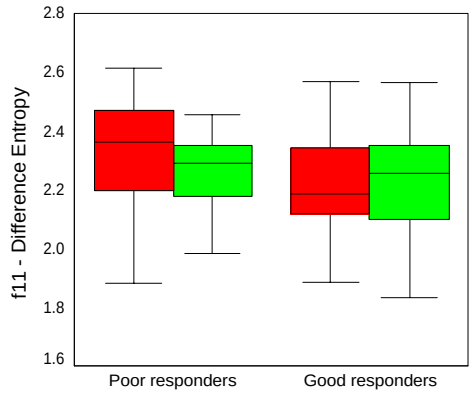
**Introduction** Preoperative chemotherapy has become a widely accepted treatment for locally advanced breast cancer. Chemotherapy can downstage the tumour and decrease its size, thus rendering patients previously thought inoperable suitable for surgery. However, a significant percentage of patients show little or no response to neoadjuvant chemotherapy. Therefore, an accurate method of rapidly assessing, or indeed predicting, tumour response would be invaluable. This would allow for the discontinuation of ineffective treatment and the switching to novel therapeutic agents. Relatively few studies exist on the accuracy of MRI in predicting residual disease after chemotherapy [1-3]. Imaging phenotype has been shown to have potential value as a predictive marker [4], confirming that radiological assessment of texture is a sensitive feature for the determination of pathology [5]. Quantitative textural analysis has recently been used to improve the specificity in MR imaging of the breast [6-7]. This work investigates the efficacy of textural analysis in predicting and evaluating breast tumour response to neoadjuvant chemotherapy.

**Methods** Forty-one women (25-76 years old, mean 50 years) with inoperable breast lesions were prospectively studied. Chemotherapy consisted of six cycles of cyclophosphamide (600 mg/m$^2$) and epirubicin (60 mg/m$^2$) at 21-day intervals and continuous infusion of 5-fluorouracil (200 mg/m$^2$/day) over 18 weeks. MR imaging was performed prior to commencement of chemotherapy (TP0), after 2 cycles of chemotherapy (TP2), and after completion of chemotherapy but prior to surgery (TPF). All imaging was performed using a GE Signa Echo-speed 1.5 T scanner and a dedicated breast coil. After contrast enhanced imaging fat suppressed post contrast data was obtained using a 3D FSPGR sequence. The voxel volume ranged from 0.46 mm$^3$ to 2.54 mm$^3$. Tumour volumes were manually segmented and ranged in size from 3.3 cm$^3$ to 234.0 cm$^3$ (1536 to 125785 pixels) at TP0. After histogram equalisation and decimation to 32 grey levels, co-occurrence matrices were calculated. Textural analysis was implemented using the spatial grey level dependence method and 14 textural measures previously defined [8] were computed for each lesion.

**Results** A significant reduction in tumour volume was noted over the time course of chemotherapy (median volume reduced from 13.2 cm$^3$ to 2.5 cm$^3$, $p<0.0001$) with larger lesions showing a greater reduction in absolute tumour volume (Pearson correlation coefficient = 0.966). Patients were separated into two groups dependent on response at TP2 – those who showed less than 50% decrease in tumour volume (20 cases) and those who showed greater than 50% decrease in tumour volume (21 cases). Significant ($p<0.05$) or borderline significant ($0.05<p<0.09$) differences were seen between the 2 groups for 11 textural parameters at TP0, but borderline differences were only seen on 2 parameters at TP2 (see table) indicating a convergence of textural features over the course of treatment (see figure). Combination of 5 textural parameters in a logistic regression model revealed a predictive accuracy of 83%.

| *Textural Parameter* | *TP0* | *TP2* |
|---|---|---|
| $f_1$-ASM | **0.066** | 0.103 |
| $f_2$-Contrast | **0.044** | 0.402 |
| $f_3$-Correlation | **0.048** | 0.381 |
| $f_4$-Variance | 0.712 | 0.471 |
| $f_5$-IDM | **0.048** | 0.286 |
| $f_6$-Sum Average | 0.091 | 0.552 |
| $f_7$-Sum Variance | **0.088** | 0.327 |
| $f_8$-Sum Entropy | 0.132 | 0.134 |
| $f_9$-Entropy | **0.071** | **0.069** |
| $f_{10}$-Difference Variance | **0.052** | 0.287 |
| $f_{11}$-Difference Entropy | **0.042** | 0.223 |
| $f_{12}$-Info. Measure of Correlation 1 | **0.067** | **0.082** |
| $f_{13}$-Info. Measure of Correlation 2 | **0.080** | 0.112 |
| $f_{14}$-Maximal Correlation Coefficient | **0.064** | 0.223 |

*P-values obtained in comparison of the textural parameters of poor and good responders at TP0 and TP2*




*Box-plot of difference entropy at TP0 (red) and TP2 (green) illustrating textural convergence*

**Discussion** Distinct differences in texture prior to treatment have been noted between lesions that showed a greater initial response, compared to those that had a poorer response. Logistic regression analysis may aid the determination of patients most suitable for neoadjuvant chemotherapy. The convergence of textural parameters at TP2 probably indicates that the remaining tissue is the most chemotherapeutic resistant.

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