EPOS™ Poster Submission

B-1088 Predicting non-response to NAC in patients with breast cancer using 3D texture analysis

ControlNr.: #6137

Keywords: Breast, Oncology, MR, MR-Diffusion/Perfusion, Computer Applications-Detection, diagnosis, Treatment effects, Cancer

Status: SUBMITTED

Type: Scientific Paper

Authors: N. Michoux[1], L. Bollondi[2], A. Depeursinge[3], A. Geissbuhler[2], L. Fellah[1], H. Müller[3], I. Leconte[1]; [1]Brussels/BE, [2]Geneva/CH, [3]Sierre/CH

SECTIONS
Coverpage
Purpose
Methods and materials
Results
Conclusion
Personal information
References
Keywords

Previous Next

Section: Purpose

Neoadjuvant chemotherapy (NAC) has a major role in the treatment of breast cancer [1,2]. However, the rate of response to NAC is limited and dependent on the subtypes of cancer [3,4]. Therefore, the identification of non-responding patients is important, especially as it may allow considering alternative therapeutic options. Pre-NAC semi-quantitative DCE-MRI parameters have been reported to be significantly different in chemosensitive and chemoresistant breast lesions [5-7]. First studies on breast MR images showed that alternative post-processing approaches such as texture analysis may help evaluate tumor response to NAC [8,9]. The aim of the study is to investigate the value of MRI texture analysis in predicting non-responders to NAC, especially in comparing the predictive performance of pre-NAC 3D texture parameters with that of pre-NAC 2D texture parameters.

Previous Next

EPOS™ Poster Submission

SECTIONS
Coverpage
Purpose
Methods and materials
Results
Conclusion
Personal information
References
Keywords

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Previous Next

Section: Methods and materials

This retrospective study was approved by our institutional ethical committee and included 70 patients. All patients had an invasive breast carcinoma diagnosed on core-biopsy specimen. To obtain a homogeneous histological sample for texture analysis, only invasive ductal carcinomas with and without ductal carcinoma in situ were included in the study. A baseline MRI as well as a pre-operative MRI to evaluate response to NAC was performed in all patients. A pathological complete response (CR) was defined as the absence of invasive and in situ cancer in breast and nodes. A partial response (PR) was defined as a decrease of invasive cancer exceeding 30%. A non-response (NR) was defined as a decrease of invasive cancer lower than 30%. At histological analysis, 15 patients were thus classified as CR, 36 as PR and 19 as NR.

MRI examinations were performed using a 1.5T whole-body imaging system (Gyroscan Intera, Philips Medical System, The Netherlands) and a breast coil. Patients were imaged in the prone position with T2-weighted and diffusion-weighted imaging (DWI) (b0, b600) sequences, and a 3D gradient echo axial T1-weighted sequence with fat suppression (SPAIR). Scan parameters were TR/TE = 4.8/2.4 ms, flip angle = 10°, FOV = 355x355 mm, matrix 320x320, slice thickness 2.5 mm, voxel size 0.65x0.65x1.25 mm after reconstruction. The anatomic study was followed by a dynamic study. Patients received 0.1 mmol/kg of gadobenate dimeglumine (Multihance, Bracco Imaging, Germany) followed by 30 mL saline flush injected at a rate of 2 mL/s with an automated injector. One pre- and five post-injection images were acquired with a temporal resolution of approximately 60 seconds. Analyses were performed on subtracted images, i.e. the residual difference image obtained after the second post-contrast image has been subtracted from the pre-contrast image.

MR images were reviewed consensually by a trainee and two experienced radiologists without knowledge of the pathological findings or mammographic and sonographic data, by using the BI-RADS MR lexicon [10] (Figure 1). Breast lesions were segmented manually on each slice of the MRI volume then recontructed in 3D (Figure 2). The intra-lesional texture was assessed as follows (Figure 3). From the grey level co-occurrence matrix (GLCM), 11 texture parameters (i.e. textons) describing the grey levels interdependence in the lesion were estimated [11]. From the run length matrix (RLM), 11 textons describing the distribution of runs of grey levels were estimated with the same computation parameters [12]. From the Riesz transform, 30 textons characterizing the important orientations and scale properties of grey levels were estimated [13]. 3-D multiscale Riesz filterbanks are advantageous for texture characterization because they quantify the local amount of directional image patterns at multiple scales. Second-order Riesz wavelets were used, yielding 6 filters per image scale that are oriented along the main image directions X, Y, Z and three diagonals XY, XZ and YZ. We hypothesized that the local morphological properties of breast tissue can be expressed as the combinations of the responses of

Sidebar

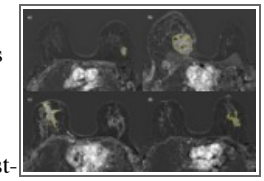

Fig. 1 : Axial subtracted images of lesions showing the largest area of the breast...

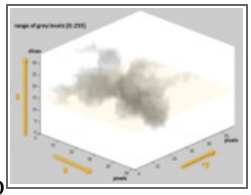

Fig. 2 : 3D volume of the breast lesion c) showed in Figure 1 reconstructed by linear...

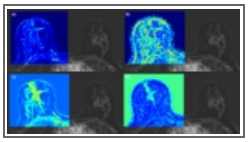

Fig. 3 : Pixel-wise analysis of the breast lesion c) showed in Figure 1. Are...

properties of breast tissue can be expressed as the combinations of the responses of the oriented filters.

The mean value (over all voxels in the lesion) of the textons was estimated. Then, two multi-parametric classifiers were used to predict the non-responders to NAC: a logistic regression model [14] and a support vector machine (SVM) model [15]. As one cannot know a priori how many and which parameters are important to the classification, all possible combinations of 2 to 5 parameters among 52 parameters) were submitted to the classifiers successively. To estimate how accurately the predictive models would perform in practice, a leave-one-out cross-validation was applied.

Previous Next

EPOS™ Poster Submission

SECTIONS
Coverpage
Purpose
Methods and materials
Results
Conclusion
Personal information
References
Keywords

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Section: Results

Previous Next

Biological and imaging parameters

Neither the mass enhancement nor the non-mass enhancement were statistically different between NR and PR+CR. NR were significantly more represented in Luminal-A subtype compared to PR+CR. NR were significantly less represented in Ki67>14% and HR-/HER2+ compared to PR+CR (non-significant trend). No statistical difference on histological grade between NR and PR+CR was observed.

Multi-parametric prediction

Computation parameters for texture analysis were: distance of one pixel between two neighboring pixels, average of the angular relationships on the thirteen main directions, four bits of grey levels. Using SVM as classifier, a predictive model relying on 3 Riesz parameters was found to perform with a predictive accuracy of 81%: Se = 47% (9/19 NR) and Sp = 94% (48/51 PR+CR). Using the logistic regression as classifier, a better model for identifying NR patients based on 5 textons (1 RLM + 4 Riesz) was found to perform with a predictive accuracy of 76%: Se = 89% (17/19 NR) and Sp = 71% (36/51 PR+CR).

Previous Next

EPOS™ Poster Submission

View

Back to Overview

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SECTIONS
Coverpage
Purpose
Methods and materials
Results
Conclusion
Personal information
References
Keywords

Section: Conclusion

Previous Next

The main result of this study is that a multi-parametric model based on textons only, i.e. without the additional contribution of morphologic, biologic or DCE-MRI parameters, was able to predict non-response to NAC with a good performance level.

Texture analysis allows assessing the spatial distribution of the grey levels in the MR image of which distribution results from underlying structural properties of tissues affected by the disease processes; a concept which has been validated by histopathological analysis [16].

The usefulness of pre-NAC texture parameters in predicting response to NAC has been proven already but based on 2D analysis of breast MR images [17]. In a pilot work, we combined kinetic and texture parameters extracted from a single subtracted MR image showing the largest area of the breast lesion with a high enhancement. Using *k*-means clustering as statistical classifier, a predictive model relying on 4 parameters (1 GLCM, 2 RLM, 1 kinetic) was found to perform with Se = 84% and Sp = 62% [18]. The predictive accuracy of the present 3D analysis is superior to that of 2D analysis (76% vs 68%). However, the gain in performance remains modest. While a predictive model based on textons only improves the practicality of the analysis, the 3D segmentation of breast lesions lengthened the processing time of MR images substantially.

These preliminary results warrant further investigations. Especially, testing alternative texture analysis techniques (multiple frequency scales [19], S-transform [20]), exploring different and larger combinations of textons with BI-RADS, kinetic and/or biologic parameters (Ki67>14%, HR-/HER2+), using other machine learning methods (since other types of classifiers than those tested in this study can be implemented, with a possible impact on the performance of the model) may help improve the predictive performance, and reach a definitive conclusion on the clinical practicality of texture analysis. The rationale behind these investigations is the development of a computer-assisted solution based on the texture analysis of MR images that may contribute to an appropriate treatment outcome for patients with breast cancer initially eligible for NAC.

Previous Next

EPOS™ Poster Submission

View

Back to Overview

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ControlNr.: #6137

SECTIONS
Coverpage
Purpose
Methods and materials
Results
Conclusion
Personal information
References
Keywords

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Section: References

Previous Next

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Previous Next

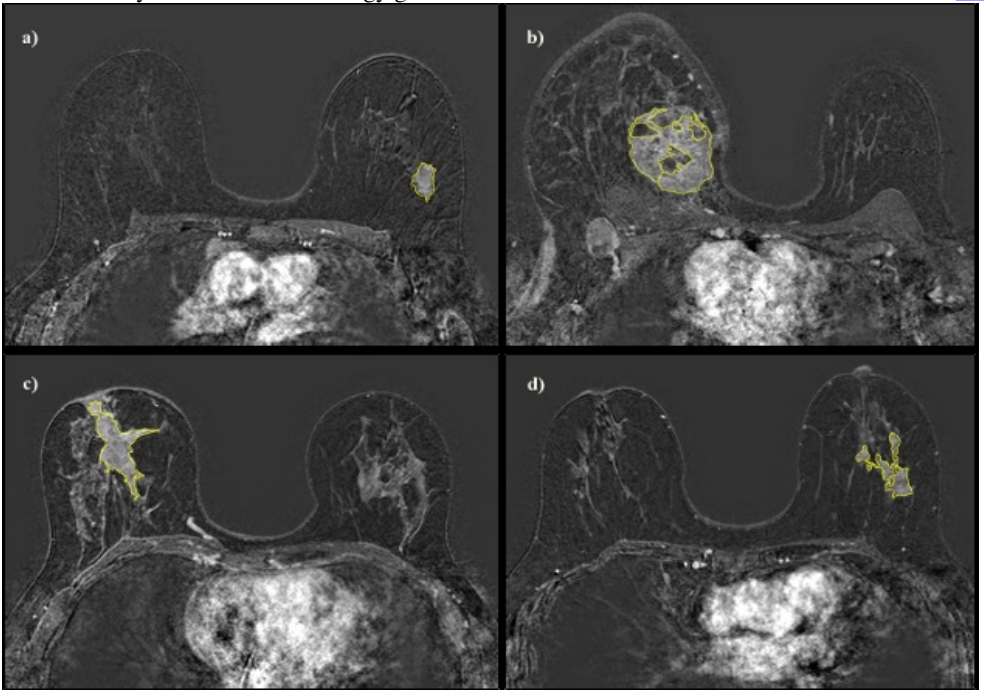

Fig. 1: Axial subtracted images of lesions showing the largest area of the breast lesion with a high enhancement (excluding macro vessels) in patients with breast cancer eligible for NAC. According to the BI-RADS MR lexicon, tumors are described as: a) oval mass with irregular margins with a homogenous enhancement, b) round mass with necrosis areas excluded from texture analysis, c) irregular mass with nipple invasion, d) regional non-mass lesion with homogeneous enhancement. Regions of interest were drawn manually on each slice of the MRI volume by two expert radiologists.

References: Department of Radiology, Université Catholique de Louvain - Cliniques Universitaires Saint-Luc - Brussels/BE

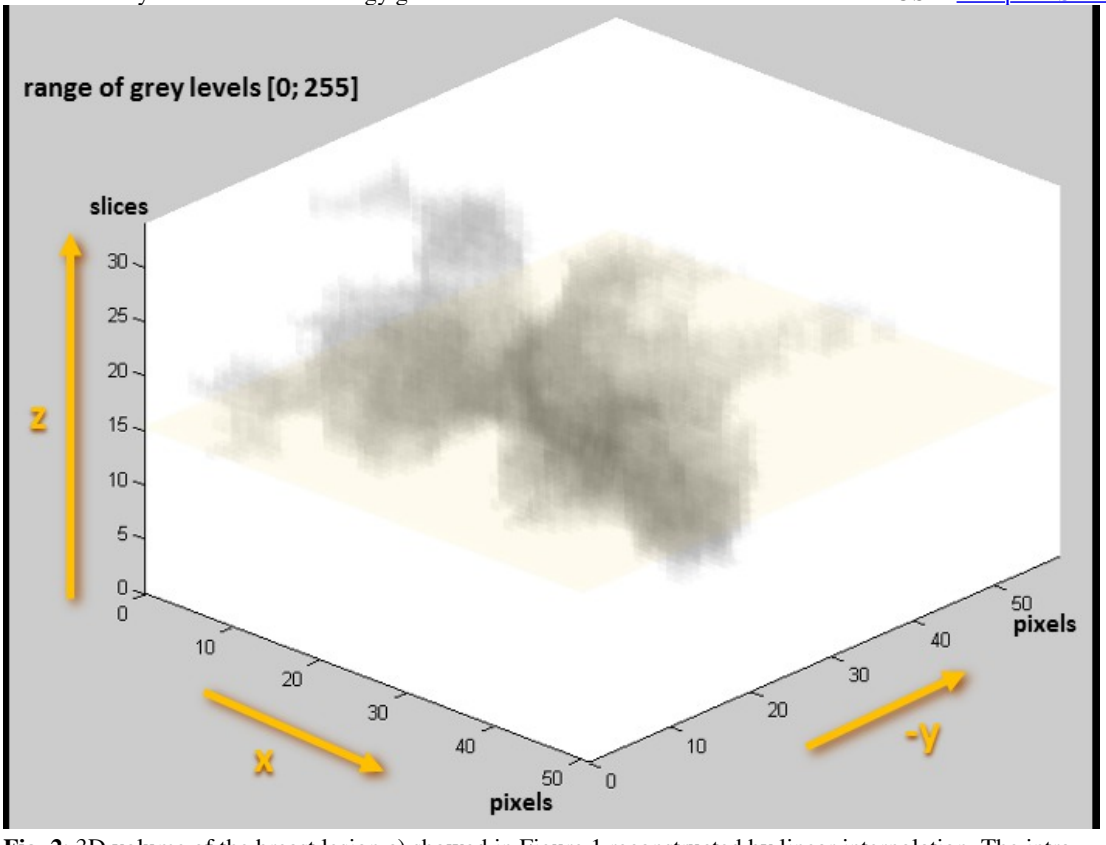

Fig. 2: 3D volume of the breast lesion c) showed in Figure 1 reconstructed by linear interpolation. The intra-lesional 3D distribution of the grey levels (i.e. the 3D texture) was then assessed using 52 texture parameters derived from GLCM, RLE and Riesz transform.

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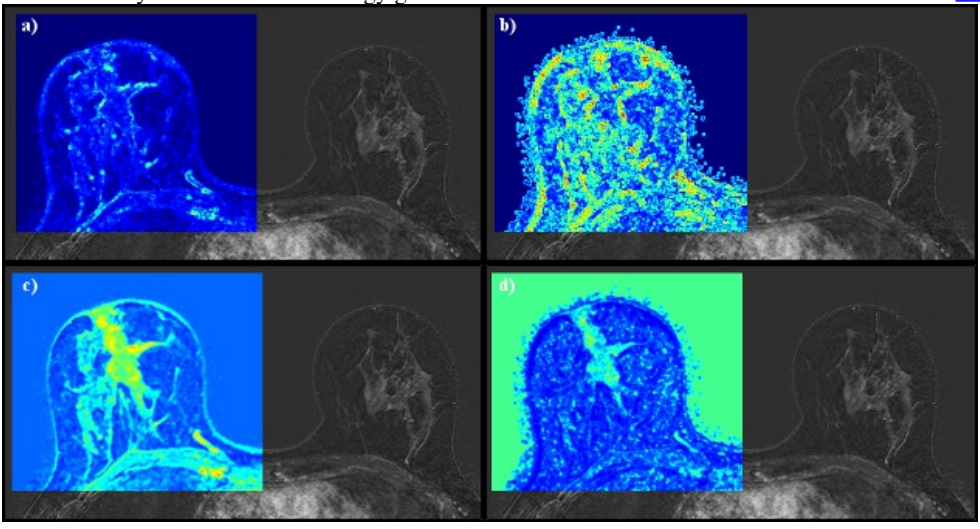

Fig. 3: Pixel-wise analysis of the breast lesion c) showed in Figure 1. Are respectively displayed, the textons a) correlation (measure of linear dependency of grey levels of neighbouring pixels), b) difference variance (measure of variation in the difference in gray levels between voxel pairs), c) sum average (measure of overall image brightness), d) sum variance (measure of how spread out the sum of the grey levels of voxel pair is) from the GLCM, with mean value estimated on a 3x3 neighborhood around the pixel of interest then normalized on the 0-255 range. This pixel-wise calculation is extended to 3D in the present study.

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