Role of Advanced MRI techniques in early detection of pathological response to neo adjuvant chemotherapy in breast cancer patients

A Thesis

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By

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LIST OF ABBREVIATIONS

ADC	Apparent Diffusion Coefficient
ALNs	Axillary Lymph Nodes
AMF	Anterior Mammary Fascia (AMF)
ASL	Anterior Suspensory Ligament (ASL)
BIRADS	Breast Imaging Reporting and Data System
BRCA1	Breast Cancer Gene 1
BRCA2	Breast Cancer Gene 2
CT	Computed Tomography
CR	Complete Response
CTH	Chemotherapy
DEC	Dynamic Enhanced Contrast
DCIS	Ductal Carcinoma in Situ
DWI	Diffusion Weighted Image
ER	Estrogen Receptor
FN	False Negative
FP	False Positive
HER2	Human Epidermal Growth Factor Receptor 2
IDC	Invasive Ductal Carcinoma
IDC-NST	Invasive Ductal Carcinoma- Non Specific Type
ILC	Invasive Lobular Carcinoma
LCIS	Lobular Carcinoma In Situ
LN	Lymph Node
LIQ	Lower Inner Quadrant
LOQ	Lower Outer Quadrant
Ki-67	Profilteartive Factor
MIP	Maximum Intensity Projection
MLH1	MutL Homolog 1
MLH2	MutL Homolog 2
MR	Magnetic Resonance
MRS	Magnetic Resonance Spectroscopy
NAC	Neo Adjuvant Chemotherapy
NACT	Neo-Adjuvant Chemo Therapy
NME	Nonmass Enhancement
NOS	Not Otherwise Specified

NST	Non Specific Type
OCL	O'clock
pCR	Pathological Complete Response
PMF	Posterior Mammary Fascia
PPM	Parts Per Million
PPV	Positive Predictive Value
PR	Progesterone Receptor
PR	Partial Response
PSL	Posterior Suspensory Ligament
PTEN	Phosphatase and Tensin Homolog
PD	Progressive Disease
PRESS	Point-Resolved Spectroscopy Sequence
RECIST	Response Evaluation Criteria In Solid Tumors
Resp.	Response
RCR	RCR Radiological Complete Response
T	Tesla
TP	Total Positive
SNR	Signal to Noise Ratio
SD	Stable Disease
STK11	Serine/Threonine Kinase 11
SV MRS	Single Voxel Magnetic Resonance Spectroscopy
tCho	Total Choline
TDLU	Terminal Ductal Lobular Unit
TN	True Negative
TP	True Positive
TP53	Tumor Protein 53
UOQ	Upper Outer Quadrant
VOI	Volume-of-Interest
WI	Weighted image

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INTRODUCTION

Neo adjuvant chemotherapy (NAC) has been increasingly utilized in the treatment of breast cancer, as the long-term distant and local-regional control of cancer provided by NAC have been reported to be similar to those offered by adjuvant chemotherapy. ***(Cho et al., 2014)***

NAC was used for treatment of locally advanced breast cancer. Nowadays, NAC is more and more used in early stages of breast cancer, for example to enable breast conserving therapy (for patients who were originally scheduled for mastectomy), to enable less complicated surgery in cases where skin or pectoral muscle is involved, or to achieve better cosmetic results after surgery. (**Lobbe *et al., 2012)***

Decisions regarding the continuation of current regimens and the appropriate type and timing of surgery depend on the radiological and clinical assessment of residual tumor size during neoadjuvant chemotherapy. Until now, many studies have shown that physical examinations, mammography and sonography provide suboptimal evaluations of lesion extent that do not allow accurate assessments of pathological response or residual tumor size **(Shin *et al*, 2011).**

Many examinations have been proposed to evaluate response monitoring in breast cancer patients receiving NAC, such as physical examination, mammography, and ultrasound. However, their accuracy was only modest. There is increasing evidence that magnetic resonance imaging (MRI) is an excellent imaging tool to monitor response to NAC, for both early response monitoring and the assessment of residual disease extent. **(Lobbe *et al., 2012)***

Early response monitoring is considered to be the monitoring of disease changes after the first cycle(s) of NAC treatment. In other words, it is the assessment of disease changes before the completion of the entire course of NAC. The MRI techniques that were most frequently used were dynamic, contrast-enhanced MRI (DCE-MRI), diffusion weighted-imaging (DWI), and MR spectroscopy (MRS). **(Lobbe *et al.*, 2012).**

Standard DCE-MRI can be used for early response monitoring. In this approach, lesion morphology and extent is assessed by evaluating contrast-enhanced, T1 weighted images and by analyzing the signal-intensity time curves in the contrast-enhanced dynamic series. Measurement of tumor diameter is perhaps the simplest method of (early) response monitoring **(Kul *et al*, 2007).**

Change of largest late enhancement diameter in the tumor on serial MRI has the potential to assess early breast cancer

response to neo adjuvant chemotherapy. In clinical practice, the MRI response prediction test may offer the oncologist an objective tool of high specificity to tailor the chemotherapy for each individual patient **(Loo *et al* , 2008).**

In breast cancer, dense packing of cells results in a restricted movement of water molecules. As a result, the ADC value decreases in DWI. During NAC, cell density of the tumor generally decreases, improving water molecule movement within the tumor. As a consequence, the ADC increases during NAC if a proper response is expected. If ADC values remain stable or even decreases further, it would be suggestive for stable or progressive disease under NAC. Thus, measurement of ADC might be a suitable parameter for evaluating treatment response. **(Woodhams *et al.*, 2010)**

In MRS, the molecular composition of a tissue of interest is analyzed by looking at the spectrum of resonances produced by the MR signal. This spectral 'signature' is used to diagnose certain metabolic disorders that are associated with tumour cells. Relative to normal breast tissue, breast cancers have increased levels of choline-containing compounds **(Lobbe's *et al*, 2012).**

Some studies have shown a decrease by 100 % in the concentration of tumoral choline following 3-4 cycles of neo adjuvant chemotherapy. **(Baek *et al*, 2009)**

AIM OF THE WORK

The purpose of this study was to determine the accuracy of MRI in early detection of pathological response after 3 cycles of neo adjuvant chemotherapy for breast cancer. That will be compared with the gold standard of post-surgical pathology.