BRÖSTCANCER FÖRBUNDET

Forskningsrapport

Huvudsökande:
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Frågeställning:
Preliminary evaluation and optimization of simultaneous digital breast tomosynthesis and mechanical imaging, DBTMI, a novel method for breast cancer screening, aimed to improve clinical accuracy and reduce recalls and unnecessary biopsies.

Tre frågor till Predrag:

Hur kan resultatet av er forskning hjälpa patienterna, rent konkret?
Early breast cancer screening saves lives. Current standard, digital mammography, DM, is limited by missed cancers and false positive, FP, detections. Novel screening methods, e.g., digital breast tomosynthesis (DBT, a 3D mammography,) improve detection but may increase FPs. As suggested by our preliminary results, combining DBT with mechanical imaging into DBTMI can improve screening accuracy, while reducing FPs and unnecessary biopsies -- which also reduce psychological burden to women and the healthcare cost.

Hur viktigt har stödet från Bröstcancerförbundet varit för er forskning?
The support from Bröstcancerförbundet (BF) was very important to my integration in LU Medicine, following my EU Marie Curie visiting fellowship and transfer from the University of Pennsylvania in USA. This funding resulted in numerous publications and awards to my students, and led to additional research grants, including 2022 Bröstcancerförbundet grant, and my recent 2024 Cancerfonden grant. Importantly, the Bröstcancerförbundet support was instrumental in my promotion to Docent at Lund University Translational Medicine in 2023!

Vad vill du hälsa alla Bröstcancerförbundets givare?
I am very grateful for the Bröstcancerförbundet support to my research, to the benefit of women in Sweden and worldwide through more accurate breast cancer screening with reduced stress and pain from biopsies, and more efficient and economical breast health care. Stort tack!

Läs gärna publikationen på följande sidor.

2020 Bröstcancerförbundet Project:

Clinical optimization of cancer screening with simultaneous DBT and mechanical imaging (MI);

PI: Predrag R Bakic, Lund University

SCIENTIFIC REPORT

My 2020 Bröstcancerförbundet Project Grant was approved with a partial budget (600 Kkr vs requested 2 562 Kkr). Thus, I focused on (i) preclinical tests based on phantoms and simulation; (ii) a pilot collection of clinical simultaneous DBT and MI (DBTMI) data, and (iii) a preliminary, limited analysis of clinical data. The following report lists major achievements – indicating modifications to the original aims. (Note: citations refer to the list of publications, submitted with this proposal.)

Aim 1: Assess and optimize DBTMI preclinically by physical phantoms and computer simulations.

Phantom studies have used (i) *DBTMI prototype system*, combining Siemens Mammomat Inspiration DBT and Tekscan pressure sensor BRE 53502; and (ii) *CIRS deformable physical breast phantom 073*.

- I ran phantom studies to test and optimize the sensor positioning procedure, to optimize the spatial matching of DBT and MI data, and to fit DBTMI acquisition into clinical workflow with minimum disruption. As result, Velcro patches were added for fast and repeatable sensor positioning.
- Phantom studies also tested the range of MI signal for various lesion types, and its reproducibility when repositioning the phantom (*Fig 1*). [16] High pressure was observed for solid tumors:18.0±1.0 kPa for centrally located tumour and 12.3±1.5 kPa for a tumour near the nipple, relative to the background (7.44±0.19 kPa). Simulated cysts did not produce high pressure.
- Currently, I use 3D printing (Ultimaker S5, by equipment grant from Malmö Cancer Center) to develop deformable test objects for calibration and testing of MI sensors.

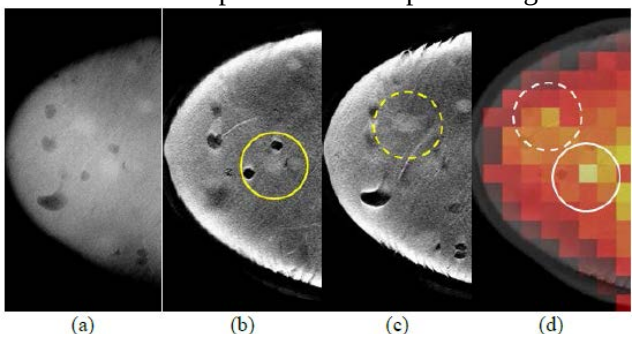
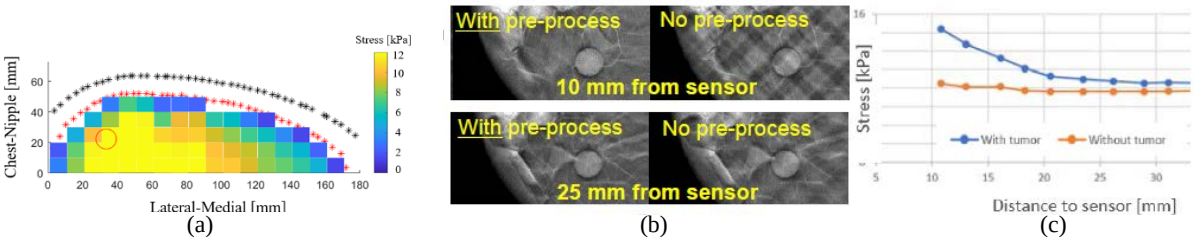


Figure 1: DBTMI of a deformable phantom. Shown are (a) the central DBT projection; reconstructed images at (b) 9mm, (c) 23mm above the sensor; and (d) MI data overlaid onto (b). *Circles show solid lesions, matching high MI (bright) in (d)*

Simulation studies have used the open source platform *OpenVCT* [53 in the list of publications] (that I developed in USA). The platform was expanded to model the MI acquisition [1, 25] and breast tumors [2,26]. Expanded platform allows virtual clinical trials (VCTs) for optimizing DBTMI and designing future clinical trials. *These simulation tools were developed by my two Master students at Lund Univ.*



(a) (b) (c)

Figure 2: Using (a) a finite element model of breast compression, and (b) virtual tumors at different depth, we calculated (c) the MI stress for different tumor depth and compared it to the phantoms with no tumors.

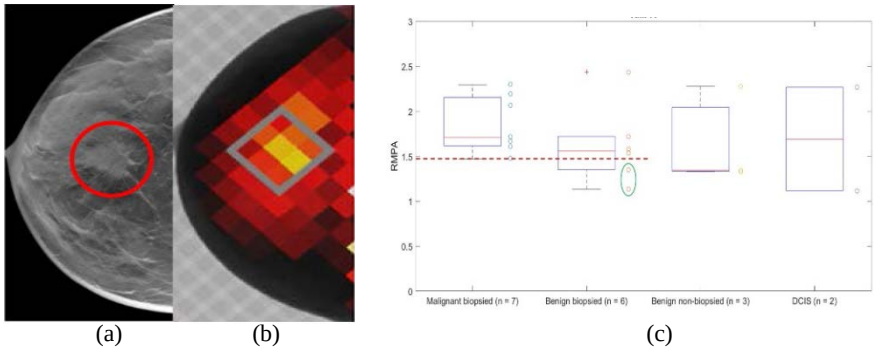
DBTMI simulation tools have been integrated into OpenVCT platform, and used in a preliminary VCT of the effects of tumor depth on DBTMI acquisition [19], *Fig 2*. Further research is ongoing, in potential optimization of the MI threshold as a function of tumor depth. This work emphasizes the advantage of simulation studies in tasks which are impractical or prohibited to perform clinically (as assessing the effects of lesions at various depth in the breast).

Deliverables: Optimized DBTMI setup using Velcro-based positioning; spatial matching of DBT and MI data; 3 journal papers [1, 2, 4] and 6 conference papers [16, 20-22,25-26]

Aim 2: Collect clinical DBTMI of 100 women recalled from screening.
Note: Originally proposed comparison of DBTMI vs DBT+US was postponed, due to the limited budget. Instead, we focused on DBTMI collection and preliminary analysis. The analysis of US reports is currently ongoing.

Pilot clinical DBTMI collection was approved in April 2021 (#Dnr 2021-606); it started in May 2021. *Initially, the collection has been slowed by the COVID-19 pandemics – which caused frequent missing appointments, and occasional radiographer staff on sick leave.*

During May-Dec 2021, collected was 101 DBTMI case. (The collection is ongoing, with the current count of 135 datasets.) Just recently (May 2022), I have expanded the collection to include an alternative DBTMI prototype system, using General Electric (GE) Pristina DBT with Tekscan pressure sensor. *I am renewing the ethics approval, to collect more clinical images, and confirm both prototypes have sufficient image quality. The goal is to collect a total of 250 DBTMI cases by the end of 2022.*



(a) (b) (c)

Figure 3: Preliminary clinical DBTMI. (a) DBT image of a malignant tumor and (b) corresponding MI. (c) MI response for 18 DBTMI cases, and suggested threshold level (…).

Preliminary analysis of the 52 collected cases was presented at the 2022 IWBI Conference, Fig 3. [17] Of 52 cases, we excluded 15 MI datasets for (i) low stress (<0.5kPa) at suspected location, or (ii) the lesion close (<1.5cm) to the chest wall or breast edge. Of 37 included DBTMI, radiologists classified 19 as normal. Fig. 3 shows 18 remaining cases: biopsy confirmed cancers (7) and DCIS (2), biopsy confirmed benign (6) and non-biopsied benign findings (3). Biopsied/non-biopsied benigns make up 9 false positive findings (FPs) from DM screening. DBT resolved 30% (3/9) of FPs without biopsy. When using MI threshold at the lowest relative stress (RPMA) of confirmed cancers, DBTMI resolved 30% (2/6) of the remaining FPs. *These preliminary results, from limited number of analyzed cases, support the trend of reducing false positives, which was suggested in the earlier DM+MI study. (Dustler 2017)*

Preliminary analysis of the exposure (= x-ray tube current [mA] × exposure time [s]) during DBTMI acquisition (Fig 4). [18] Based upon 20 women in our clinical observational study, we compared the breast thickness, kVp, and exposure between the DBTMI and the corresponding diagnostic DBT images. The breast thickness change due to repositioning was negligible (1.5% on average), as well as the change in kVp. There was a significant difference in exposure between DBT and DBTMI (10.1% increase, on average, p=0.00014). The exposure increase can be explained by the MI sensor structure with metallic strips and plastic coating. Further dose assessment in ongoing, with the use of physical phantoms.

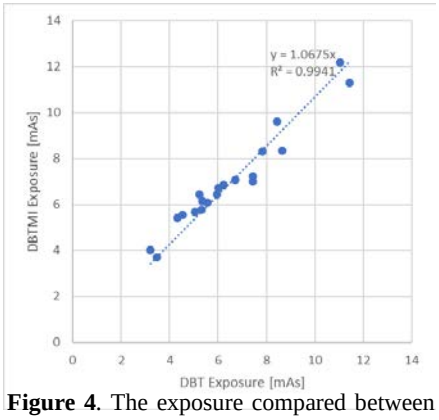


Figure 4. The exposure compared between DBTMI and DBT for 20 women recalled from mammographic screening.

Deliverables: Database of clinical DBTMI and corresponding diagnostic DBT data; 2 conference papers [17, 18]; the analysis of all 101 collected clinical DBTMI cases is currently being prepared.
In addition, pending is one journal paper on the analysis of clinical DBT data [15]

(Note: Originally proposed exploratory Aim 3 to assess potential correlation between DBTMI tumor descriptors and histopathological characteristics, was postponed due to limited budget. It is now a separate Aim of my current continuation BF application.)