VIRTUAL CLINICAL TRIALS OF BREAST TOMOSYNTHESIS

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Abstract: Validation of novel x-ray breast image acquisition or analysis systems, based upon the clinical trials, is limited in terms of their cost, duration, and repeated exposure. These limitations have been emphasized by the emergence of digital breast tomosynthesis and breast computed tomography due to their large number of system settings to be tested. Virtual clinical trials have been introduced as alternative preclinical validation, through the modeling of breast anatomy, image acquisition and analysis. This presentation illustrates the development of an automated simulation platform for virtual clinical trials of breast tomosynthesis cancer screening. The advantages and limitations of the current approach are discussed, as well as its extension to other virtual trials, including the validation of methods for dose reduction in clinical imaging exams.

Keywords: Virtual clinical trials, software breast phantoms, real-time simulation, digital breast tomosynthesis, breast cancer screening.

Introduction: Digital breast tomosynthesis (DBT) is a 3D x-ray breast imaging modality, based upon the tomographic reconstruction of breast volume from a series of projections acquired within a limited angle of the x-ray tube [1]. Breast tissue structures contained within a plane of reconstruction are shown in focus, while the out-of-plane structures are suppressed. This yields an improved image quality relative to 2D mammography by reducing the anatomical noise caused by the overlapped projections of normal breast anatomy. DBT systems have been approved for clinical use in the US since 2011. The Hospital of the University of Pennsylvania (Penn) is among several institutions which has included DBT into their breast screening protocols [2].

The clinical approval and further optimization of DBT and other novel imaging systems require the use of clinical imaging trials for the validation and comparison with existing systems. Such clinical trials are long and expensive, they include a large number of women and repeated use of ionizing radiation to obtain multiple images of the same women. Such limitations impede faster acceptance of novel imaging systems into the clinical practice. Our X-ray Physics Lab at Penn has extensive experience in developing an alternative to preclinical validation in the form of Virtual Clinical Trials (VCTs) [3]. VCTs are based upon the simulation of normal breast anatomy using software phantoms [4-6], insertion of simulated abnormalities, modeling of breast positioning, image acquisition, processing, and display, and the use of mathematical model observers for image interpretation. Preclinical VCTs can be used for identifying the most promising system setups to be tested in a focused clinical trial, thus improving the efficiency of the breast imaging system validation.

Methodology: Fig. 1 shows the principal modules of the simulation pipeline developed at Penn to support observer trials (human or model) or quantitative analysis of phantom simulated breast images. The pipeline modules are connected by an XML parsimonious data representation, which controls the data flow based upon the user specifications. In addition to basic pipeline modules, external components may be incorporated as plugins, providing flexibility for a wide range of pipeline users.
We have made efforts to accelerate phantom generation, for support of VCTs with large number of simulated anatomies or small voxel size. Currently, the phantoms are generated by recursive partitioning using octrees, with minimum computational complexity [6], and an efficient OpenCL GPU parallel implementation [7].

**Results:** Fig. 2 illustrates real-time phantom generation, by comparing the duration of different implementations of the Penn anatomy simulation method. The current implementation is capable of generating phantoms at a rate of 6-10 per minute [7]. Fig. 3 shows examples of breast phantom sections and corresponding simulated projections and reconstructed DBT images. Each voxel in reconstructed DBT slices (e.g., Fig. 3, right), corresponds to a voxel in the original phantom array (Fig. 3, left), which provides the ground truth about simulated anatomy for quantitative assessment of image acquisition, (e.g., DBT reconstruction [8]) or image analysis (e.g., denoising for dose reduction [9]).

![Figure 2 – Illustration of the real time phantom generation. Shown is the simulation time vs. phantom voxel size.](image)

![Figure 3 – Examples of a phantom section (left) and the corresponding projection (center) and reconstructed DBT image (right).](image)

**Conclusions:** VCTs of breast imaging offer preclinical validation and optimization of novel breast image acquisition systems and/or image analysis methods.

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