Aperture size selection for improved brain tumor detection and quantification in multi-pinhole ^{123}I-CLINDE SPECT imaging

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***Abstract*—A next-generation multi-pinhole system dedicated to brain SPECT imaging is being constructed by our research team, which we call *AdaptiSPECT-C*. In the current prototype, the system consists of 25 square detector modules and a total of 125 apertures grouped by 5 per module. The system is specifically designed for multi-purpose brain imaging and capable of adapting in real-time each aperture size and whether it is open or shuttered closed. The use of such system would provide optimum high-performance patient-personalized imaging for a wide range of brain imaging tasks. In this work we investigated the effect of pinhole diameter variation on spherical tumor detection and quantification for the new brain tumor imaging agent ^{123}I-CLINDE. To establish the range of aperture sizes to be investigated and to assess the quality of the images reconstructed for the different aperture sizes, we used a customized multiple-sphere tumor phantom derived from the XCAT software with a tumor size varying from 0.8 to 2 cm in diameter. Our results suggest through quantification and visual inspection that an aperture diameter in the range of 2 to 6 mm in diameter for the adaptive AdaptiSPECT-C system is likely the most suited for high performance brain tumor ^{123}I-CLINDE imaging. In addition, our study concludes that a 4 mm pinhole diameter given its excellent spatial-resolution-to-sensitivity trade-off is promising for scout acquisition in localizing target tumor regions within the brain. By exploiting the adaptive capability of the system, lower aperture size of 2 mm diameter might be of interest for optimum higher-resolution imaging of the tumor volumes. We have initiated a task-based performance of the tumor detection accuracy for a range of simulated tumor sizes using the channelized non-pre-whitening (CNPW) matched-filter scanning-observer.**

***Index Terms*—^{123}I-CLINDE SPECT imaging, glioma, next-generation clinical system, GATE Monte-Carlo simulation, pinhole diameter selection, quantification**

I. Introduction

Brain imaging with ^{99m}Tc-DTPA/-TF/-MIBI, ^{201}Tl-thallous chloride, and ^{67}Ga-citrate agents has been established as a useful tool for localization of cerebral tumors, such as gliomas, and for distinguishing tumor recurrence from radiotherapy-induced necrosis [1], [2]. Recent studies have shown that ^{123}I-CLINDE is promising tumor imaging agent due to its high tumor affinity. It could even further improve diagnosis and treatment monitoring of gliomas. In addition, it was demonstrated that ^{123}I-CLINDE is less susceptible to changes in blood–brain barrier permeability than the amino acid PET tracer ^{18}F-FET, for which increased uptake has been reported in non-tumor tissues, such as ischemia, hematoma, and radiation induced regions [3]–[5]. We are constructing an innovative static multi-pinhole SPECT system with adaptable imaging characteristics, called AdaptiSPECT-C [6], [7]. We propose in this work to determine through numerical observer and quantification studies the effect of aperture variation on the detection and quantitative accuracies of different size and contrast simulated tumors for high-performance ^{123}I-CLINDE imaging.

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II. Material and Methods

A. Description of the AdaptiSPECT-C system prototype

The current *AdaptiSPECT-C* prototype consists of 25 square detector modules of 184 by 184 mm^2 placed along 3 rings around the patient's head. Each module is irradiated by 1 direct and 4 oblique pinholes, the size of which can be adapted to the imaging task (*e.g* estimating the tumor size, contrast, shape, and/or localization). Due to high level of overlaps between the pinhole projections, opening the 5 pinholes simultaneously requires de-multiplexing which is evaluated in [8]. Thus, for the purpose of this study, we considered a single acquisition scheme consisting of solely the 4 oblique pinholes opened. For GATE simulations [9] we modeled a back-scattering compartment which allowed modeling of down-scatter interactions from ^{123}I high-energy photons with the light detecting and electrical components behind the NaI(Tl) crystal.

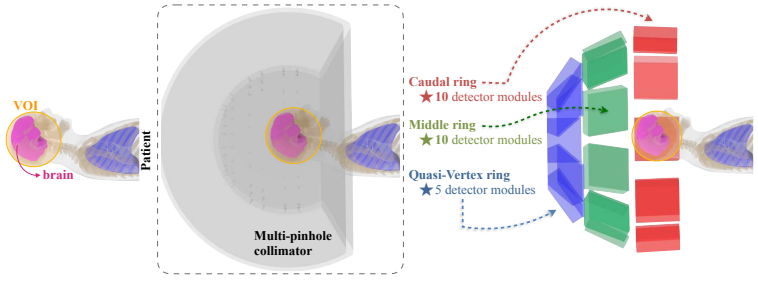

Fig. 1. Current prototype of the AdaptiSPECT-C system.

B. GATE simulation study

Each adaptable pinhole is controlled in size by a mechanical device allowing a total of 3 diameter configurations [7]. Using task-based performance of the detection task for a range of simulated tumor sizes we will determine detection accuracy using the channelized non-pre-whitening (CNPW) matched-filter scanning observer which has been found to correlate well with human observers for a range of pinhole diameters varying from 1 to 8 mm [10]. In this initial study, we assessed the image quality and quantitative accuracy provided by this range of aperture size. An approach developed in our group for modeling the system response using GATE Monte Carlo simulation, was employed to compute efficiently and accurately the system matrix for reconstruction [11]. To establish the range of aperture sizes to be investigated and to assess the quality of the images reconstructed for the different aperture sizes, we used a customized multiple-sphere tumor phantom derived from the XCAT software [12]. It consists of spherical tumors spatially distributed within the brain. The distance between each tumor center is equal to 2 times the tumor diameter. We considered a range of tumor sizes varying from 0.8 to 2 cm in diameter, which was selected on the basis it corresponds to the typical range of measurable tumor sizes seen in clinics [13]. We selected two tumor-to-background uptake ratios, 1.8 and 3.4, defining the typical range in contrast for ^{123}I-CLINDE imaging [4]. The brain uptake level was set to 1, the head to ¼ of that (0.25).

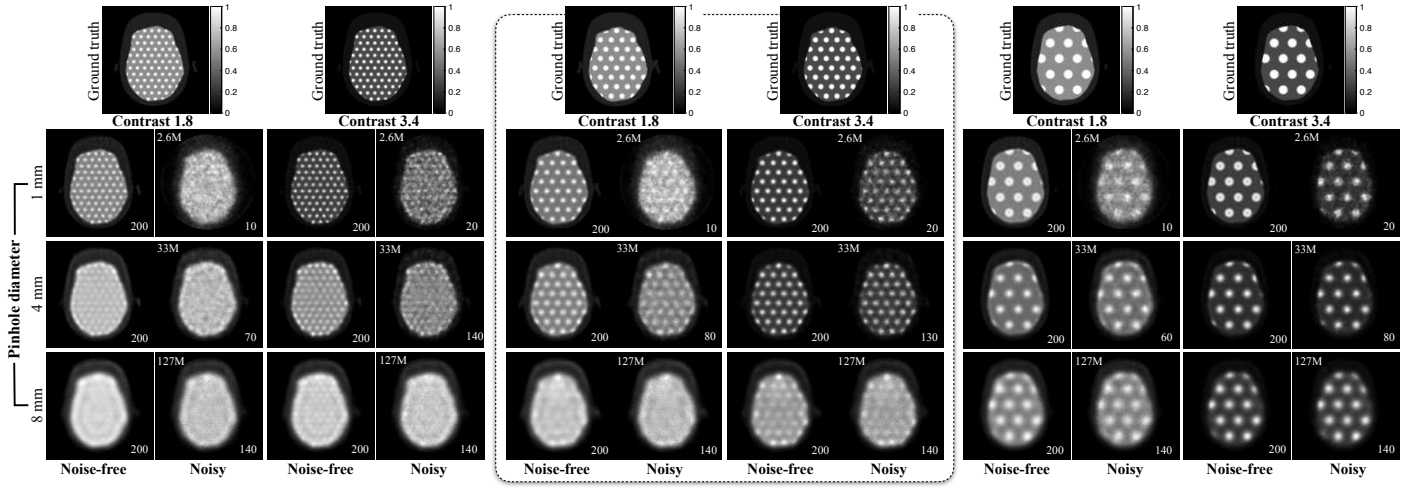

Fig. 2. Reconstructed images of the brain tumor phantom for the lowest NRMSE obtained over the number of iterations using different pinhole diameters, three tumor sizes (0.8 cm (left), 1.2 cm (middle) and 2 cm (right)), two tumor contrasts (1.8/3.4) and two noise levels (noise-free/noisy). The iteration number and the count level are shown in the lower right and upper left corners of the images, respectively.

The phantoms were simulated as being imaged following two schemes: (*i*) a first noise-free simulation for which projection data were obtained directly from the system matrices (*ii*) an equal imaging time comparison based on the simulated sensitivity compared to clinical imaging. For the second scenario, the total number of counts for the 1, 2, 4, 6, and 8 mm pinhole diameters considered, were respectively 2.6M, 11M, 33M, 72M, and 127M counts. Projections were reconstructed with 3D-MLEM into images of 120^3 voxels of $(2\ \text{mm})^3$ and the reconstruction were compared to the ground truth image. The bias, normalized root mean squared error (NRMSE) as well as the percentage of activity recovery (%AR) and contrast recovery (%CRC) were used to evaluate the image quality.

III. Results and Discussion

For noise-free data, as the pinhole diameter decreases and the tumor size increases, image quality is significantly improved both visually and quantitively (Fig. 2). The lowest NRMSE, bias, %AR, and %CRC values are reached for a 1 mm diameter for the 3 tumor sizes investigated (Fig. 3). Despite promising imaging performance suggested by the noise-free scenario, for a typical clinical acquisition, severe image quality degradation can be seen in presence of noise and as tumor contrast and size reduces. In addition, bias and NRMSE increased with higher statistical noise. While reaching excellent spatial resolution at the expense of low sensitivity, a 1-mm pinhole diameter appears to be limited for glioma imaging even for the largest tumor size. Nonetheless, de-noising or filtering techniques could help to better control the statistical noise. While providing high sensitivity, an 8-mm diameter leads to poor image quality for tumor sizes smaller than 2 cm due to significant loss of spatial resolution. However, the high sensitivity reached could be of interest for pharmacokinetic studies. For a clinical acquisition, quantitative assessment of the bias and NRMSE showed the lowest values are obtained for an aperture diameter of 2 to 4 mm. For this size range and for tumor sizes larger than 1.2 cm, a plateau is reached in terms of %AR and %CRC. Further aperture size decreases or increases do not improve the results, but instead severely degrades bias and NRMSE. Due to an excellent spatial-resolution-sensitivity trade-off, a 4-mm diameter appears both visually and quantitatively the most adequate for a tumor sizes varying from 1 to 2 cm as observed typically in the clinic. Such aperture size seems promising for a scout acquisition to localizing tumor regions within the brain, after which higher-resolution apertures (2 mm diameter) could be used for optimum imaging of the target regions. Our initial results suggest that a diameter of 2 mm should be the lowest aperture size to consider to the extent that no de-noising or filtering approaches for controlling noise are used.

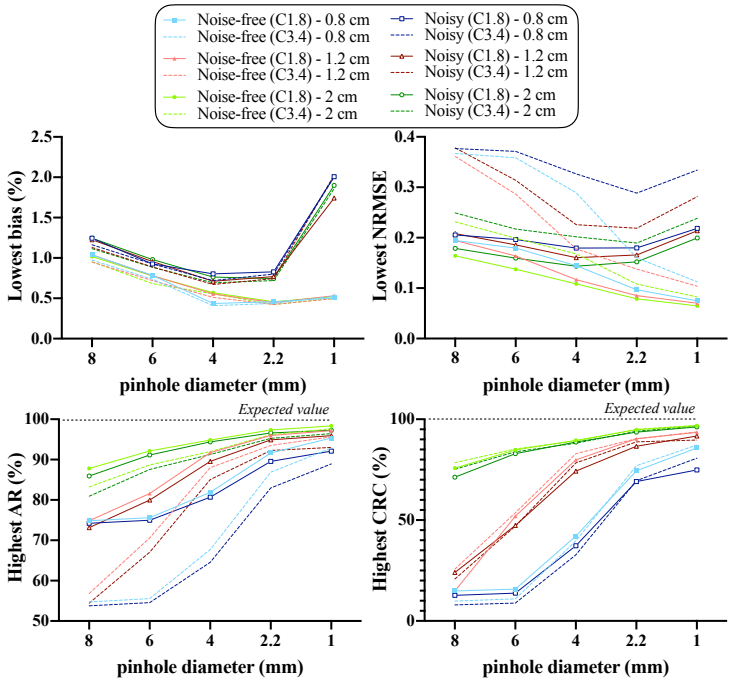

Fig. 3. Lowest bias and NRMSE and highest %AR and %CRC values over iterations using different pinhole diameters (1, 2.2, 4, 6, and 8 mm), three tumor sizes (0.8, 1.2, and 2 cm), two tumor contrasts (1.8/3.4) and two noise levels (noise-free/noisy).

IV. Conclusion and Future Prospects

In this work, we observed through quantification and visual inspection that an aperture size varying from 2 to 6 mm in diameter for the adaptive *AdaptiSPECT-C* system might be the most suited for high performance brain tumor ^{123}I-CLINDE imaging. This range of sizes will be investigated in our detection-task-performance studies.

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