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Original Article

Development of a novel linearly-filled Derenzo microPET phantom

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Abstract: Positron emission tomography (PET) phantoms are used to calibrate PET scanners so that inter-scanner and inter-isotope comparison can be made between PET datasets. Hot rod style phantoms have a hole pattern, which is filled with a positron-emitting isotope and typically involves using two radioisotope reservoirs with the pattern created with channels in between. However, this configuration is difficult to fill and requires an excess of activity and volume. Here we present an alternative design, a phantom that is linearly filled-one channel at a time. The process of fabrication of prototypes of the design is described and PET images of the prototyped phantom are also shown for a variety of commonly used radioisotopes (^{52}Mn, ^{64}Cu, ^{76}Br, ^{124}I). This design allows for a large reduction in isotope volume and required filling time making a quality assurance (QA) protocol safer, more efficient and less costly.

Keywords: Positron emission tomography (PET), quality control (QC), Derenzo phantom, rresolution, hot-rod Derenzo, microPET, 3D printing

Introduction

Small animal positron emission tomography (PET) imaging is widely used for development of preclinical diagnostic agents and the identification of therapeutic markers [1-4]. In order to compare results between institutions or between agents labeled with different PET isotopes, scanners must be well calibrated and characterized. Several standard PET phantoms allow for inter-scanner or inter-isotope comparison. One of the most common quality control phantoms for nuclear medicine imaging is the Derenzo phantom [5]. The phantom pattern, shown in **Figure 1**, is a series of positron emitting rods separated by twice their diameter in a triangular close-packed configuration. Several rod diameters are typically employed as a way to determine the diameter at which resolution breakdown occurs.

Derenzo phantoms are typically constructed by using two reservoirs of positron emitting isotopes in solution connected by channels making up the Derenzo design. In microPET versions of this design, some channels may be less than 1 mm in diameter making it challenging to displace air bubbles when filling. One approach is to employ surfactants in the isotope solution to help with channel filling. This technique is still prone to difficulties, as surfactants in the form of detergents are prone to foaming, and organic surfactants often degrade the plastic materials from which the phantom is constructed. Another method might employ creating a vacuum within the phantom volume before filling with the isotope solution, but this adds unnecessary complexity to the filling process.

One solution to the problem of properly filling every hole in Derenzo-style phantoms would be to design a phantom that is filled linearly, one hole at a time. This could be accomplished by creating a fluid path that snaked through a block of material by starting with a hole, then connecting it to an adjacent hole with a connecting channel on one side, connecting it to a third hole on the opposite side and continuing

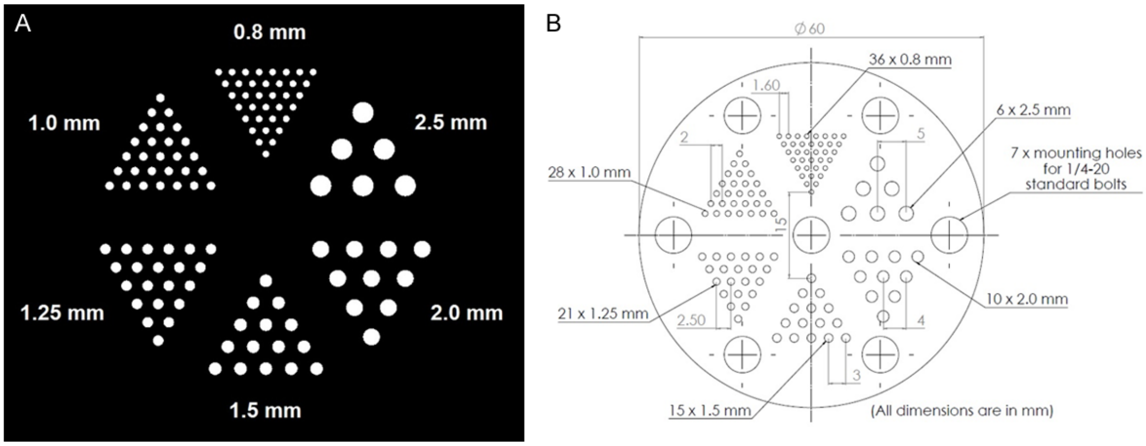

Figure 1. Cross-section of the Derenzo hole pattern incorporated into the prototype phantoms, shown with the activity highlighted (A) and in a technical drawing format to demonstrate how it is incorporated relative to the rest of the phantom (B).

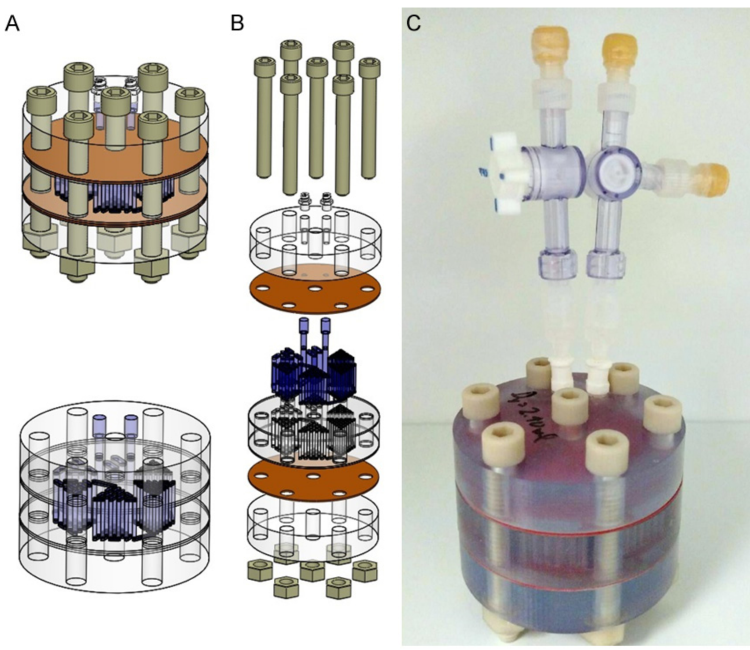

Figure 2. 3D Computer rendering of the phantom design showing all components and a rendering of the phantom design with the glass-filled nylon bolts, nuts and silicone gaskets hidden to improve visualization of the fluid volume within the phantom (A), exploded view of the phantom assembly (B) and a picture of one of the initial prototype phantoms, including the 3-way valves used during filling (C).

until all the pattern holes are filled. Such a phantom would have the additional benefit of eliminating the reservoirs used in traditional filling of these phantoms. This would reduce the overall activity needed to fill the phantom, both reducing the dose to anybody handling the phantom and increasing the quality of the resulting images by reducing noise from out-of-slice radioactivity.

Taking advantage of recent advances in three-dimensional (3D) printing [6, 7], an initial design was investigated with the fluid path winding through a single block of material. However, clearing such a long channel and cleaning out extra material from the resulting prototype, made this design impractical. Here we describe the design of a modular phantom that is filled in a linear fashion. It consists of three main pieces, a central piece, containing a hole pattern and connecting channels, and two end pieces. The piecewise design is such that it is possible to machine each component out of any desired material or use 3D printing for fabrication while still preserving the benefits of linear filling. Also shown are PET images of the hole pattern of initial prototypes of this phantom, filled with several commonly used PET isotopes in solution.

Materials and methods

Design and fabrication

All elements of the phantom assembly were designed using SolidWorks (Dassault Systémes,

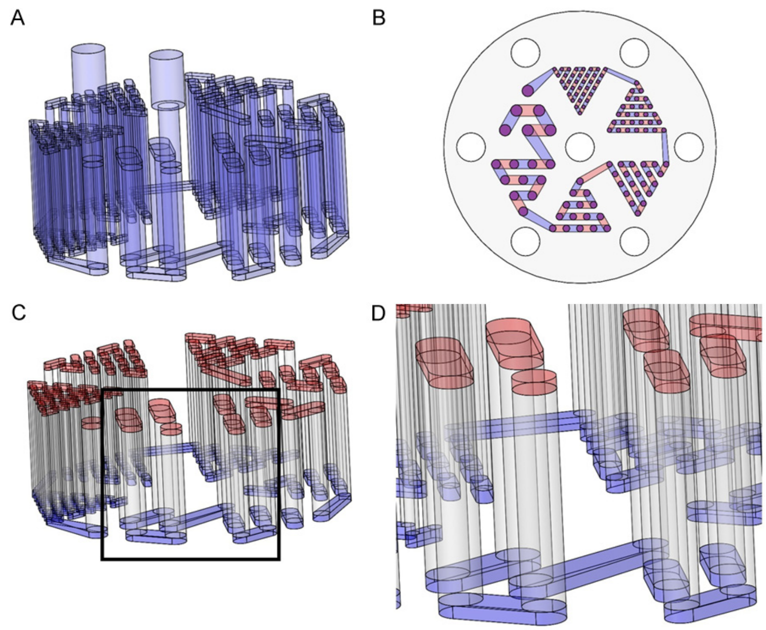

Figure 3. Computer rendering of the water volume within the initial prototype phantoms, including the inlet and outlet (A), a top view of the phantom with the water path through the phantom highlighted, with blue connections on one side of the phantom and red ones on the other (B), a computer rendering of the fluid path without the inlet and outlet and colored to illustrate the top and bottom connections (C) and a zoomed in view of the region indicated by the black box (D).

Vélizy-Villacoublay, France), a computer-aided design (CAD) software package. The overall design of the phantom is illustrated in **Figure 2**. The central piece and two end pieces for the initial prototypes were fabricated using 3D printing on a Viper Si2 stereolithography machine (3D Systems, Rock Hill, SC, USA). The two gaskets were laser cut using a PLS 6.75 laser cutter (Universal Laser Systems, Scottsdale, AZ, USA) out of silicone sheets (McMaster-Carr, Elmhurst, IL, USA). The phantom itself is held together and sealed using glass-filled nylon nuts and bolts (McMaster-Carr).

Filling

To facilitate filling of the phantom, an inlet and an outlet are incorporated into one of the end pieces of the phantom. In the initial prototypes, these were tapped and fitted with male Luer Lock fittings that could accept syringes. A Luer Lock syringe was filled with the appropriate volume and activity and fitted to the inlet of the phantom. An outlet syringe was used as well for waste collection and to eliminate leaking. A three-way valve was used between the syringe and Luer Lock at both the inlet and outlet, so that the syringes could be removed after filling. A schematic of the filling path is shown in **Figure 3**.

PET imaging

The phantom prototypes were filled with ^{52}Mn, ^{64}Cu, ^{76}Br and ^{124}I in aqueous solutions and a static PET scan was acquired on an Inveon MicroPET scanner (Siemens Healthcare, Erlangen, Germany). Greater than 400 million counts were acquired for each isotope using a 350-650 keV energy window and a 3.432 ns timing window. Isotopes were purchased commercially or produced in-house as previously described [8-10]. Images were reconstructed by three-dimensional ordered subset expectation value maximization (OSEM3D) using a 512× 512 grid size.

Results

Design and fabrication

Four initial prototypes of the final phantom design were created and assembled. To ensure proper coupling of the pieces in the assembled phantom, the mating sides of the three main phantom pieces were sanded with a series of sandpaper grits. The inlet and outlet holes were tapped to allow for the addition of male Luer Lock fittings. A photograph of the completed assembly of one of the prototypes is shown in **Figure 2**.

Filling

The phantom volume was found to be approximately 2.4 mL for all four prototype phantoms. This allowed the phantoms to be filled by drawing a small volume of radioactivity into a 5 mL Leur lock syringe, then drawing deionized water for a total volume of 2.4 mL in the syringe. The syringe would then be locked on the inlet port with a waste syringe on the outlet. Filling was rapid with minimal back-pressure. With the cor-

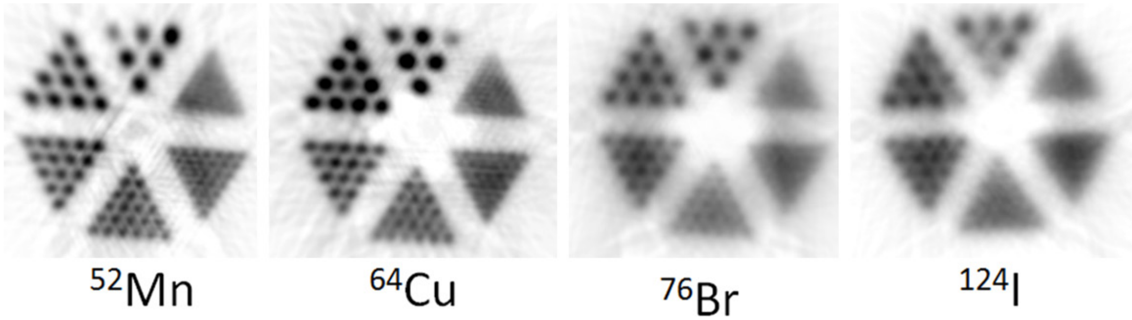

Figure 4. Images of the microPET phantom filled with ^{52}Mn, ^{64}Cu, ^{76}Br, and ^{124}I. Images were acquired on a Siemens Inveon MicroPET, and were reconstructed by OSEM3D.

Table 1. Measured hole pattern resolutions using ^{52}Mn, ^{64}Cu, ^{89}Zr, and ^{124}I on Siemens Inveon MicroPET scanner in a linearly filled Derenzo phantom, and their mean positron energies

Isotope	Smallest Resolvable Hole Pattern	Mean β^+ Energy
^{52}Mn	1.00 mm	242 keV
^{64}Cu	1.00 mm	278 keV
^{89}Zr	1.25 mm	470 keV
^{124}I	1.50 mm	820 keV

rect activity volume and filling procedure no leaks occurred.

PET imaging

PET data were acquired with ^{52}Mn, ^{64}Cu, ^{76}Br, and ^{124}I, and were reconstructed by OSEM3D. Axial slices along the pattern length were averaged to provide the images shown in **Figure 4**. With scan parameters held constant, several factors can cause inter-isotope image quality variability, including positron range and confounding gamma emissions [11, 12]. ^{52}Mn and ^{64}Cu were found to provide the best image quality with their resolutions failing between hole diameters 0.80-1.00 mm. ^{76}Br was found to have the next best resolution failing between 1.00-1.25 mm. ^{124}I was found to have the worse image quality with the resolution failing between 1.25-1.50 mm. These results are summarized in **Table 1**.

Discussion

In this work we have demonstrated a design for the successful linear filling of a Derenzo-style hot rod microPET phantom. Linear filling makes filling phantoms of this type much easier and also without bubbles that otherwise could ruin the resulting images. This method for filling phantoms is not limited to Derenzo-style microPET phantoms. It could easily be translated to any type of phantom that utilizes a pattern of filled voids. This could include other resolution phantoms, contrast detail phantoms and uniformity phantoms, for both clinical and preclinical applications.

In addition to the linear filling of this phantom design, another key aspect is its modularity. The modularity of this design did require the use of a number of bolts to assemble the phantom, which does represent a slight drawback. The bolts that were used in the prototypes were made of glass-filled nylon to provide enough compression to adequately seal the phantom. These bolts could lead to attenuation artifacts, although we did not observe artifacts in our reconstructed images.

The benefit of the modular design, however, is that it allows for ease of disassembly and cleaning and also allows each piece to be fabricated in a variety of ways including 3D printing as well as conventional machining techniques. While 3D printing allows for fast fabrication of prototypes and flexibility in design, a limitation is its accuracy, which depends largely on the material and printer used. This limitation can be overcome by using conventional machining techniques with a variety of materials. These techniques inherently produce parts with much higher spatial accuracy. The ability for this design to be manufactured with either 3D printing or conventional machining allows for both

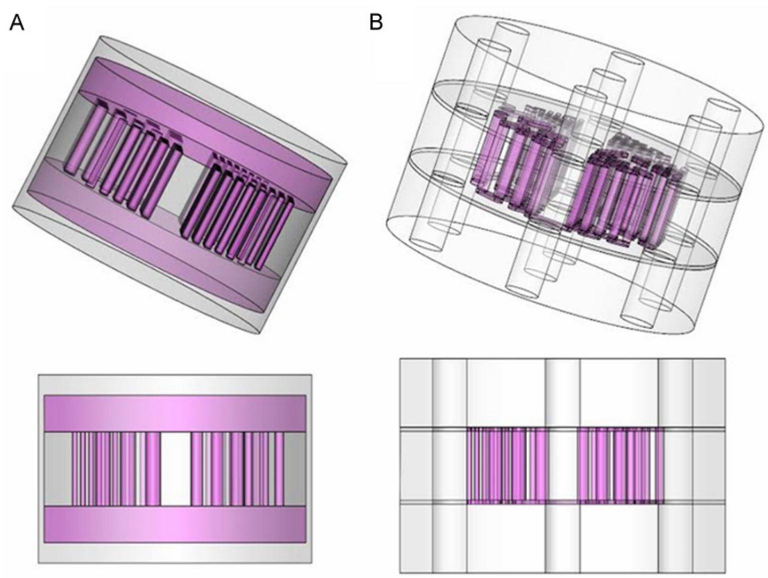

Figure 5. Illustration comparing a conventionally filled Derenzo style hot rod phantom (A) to the linearly filled phantom described in this manuscript (B). An isometric view (top) and a side view (bottom) are shown in both cases, with the fluid depicted in pink. The reduction in required fluid from the elimination of the reservoirs above and below the hole pattern in the conventional case is readily apparent.

iterative designs of new hole patterns as well as industrial-scale manufacturing.

A major benefit of the design is the reduction in activity volume required for phantom filling, illustrated in **Figure 5**. This feature reduces isotope cost, personnel handling dose and noise from out-of-slice activity. A conservative estimate of the reduction in dose can be calculated by making a few assumptions. The whole pattern shown is approximately 40 mm in diameter, and assuming a reservoir thickness of 5 mm on each side, the total activity volume for a conventional phantom would be about 14.4 mL. This corresponds to a factor of six increase in activity volume compared to the design presented here. Therefore, incorporating a phantom like the one described here into the quality assurance (QA) protocol of an imaging facility will make the QA protocol cheaper, safer and more efficient. This constitutes a significant improvement over conventional Derenzo phantom designs.

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Disclosure of conflict of interest

The method described in this paper has been filed as a patent application to the US Patent and Trade Office by the Wisconsin Alumni Research Foundation (WARF).

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