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 CIS II: Group 4

Critical Review

“Initial Testing of a 3D Printed Perfusion Phantom Using Digital Subtraction Angiography”

The paper discussed in this seminar describes the development of a 3D-printed perfusion phantom to standardize the protocol associated with existing CT-perfusion systems. Standardization of typical CT-perfusion parameters vary significantly between vendors and even the software provided to analyze the dataset. Wood created a systematic way to assess the reliability of existing perfusion systems using a reproducible and simple perfusion phantom.

One use of CT perfusion systems is for the detection of ischemic stroke. Stroke is the fourth leading cause of death in the United States and occurs when there is an interruption of blood flow to the brain, hindering oxygen for brain activities. About 2 million neurons become damaged every minute post stroke and thus the diagnosis time is a critical factor in stroke evaluation. CT perfusion imaging techniques use a contrast agent, usually composed of an iodine mixture to assist clinicians in visualizing the site of an ischemic stroke. Lack of this contrast agent signal indicates that the blood supply to the tissue is nearly zero. This area of the brain is labeled the ischemic core. Low signal indicates that the blood supply is quenched, but salvageable. This part of the brain is labeled penumbra. It is critical for clinicians to accurately determine the size and location of the penumbra to successfully treat patients. Thrombolytics is a common source of treatment. These different affected regions of the brain can be categorized using common perfusion parameters. The first parameter, cerebral blood flow (CBF) describes the blood flowing through a unit mass of brain per unit time. In normal tissue, CBF ranges from 60 to 100 ml/min/100 g. In the penumbra, 12 to 25 ml/min/100 g, and in the ischemic core less than 10 ml/min/100 g. The second parameter, cerebral blood volume (CBV) describes the volume of blood present per unit volume of brain. The third parameter, mean transit time (MTT) describes the average time for blood to flow through a region of brain. These parameters can be standardized for a given perfusion system and used to accurately diagnose affected areas of ischemic stroke.

 Existing perfusion phantom have been developed in the past such as the Driscoll phantom and the Kevin phantom but both do not physiologically represent brain capillary size. Wood chose to create capillaries that are on the same magnitude scale as human brain capillaries to accurately mimic brain tissue. 3D printing is a valid method of reproducing these micro channels. Wood used a Polyjet 3D printer Objet Eden260 V (Rehovot, ISRAEL) to print her phantom. The phantom was cylindrically shaped with diameter of 20 mm and had lengths of 20 and 30 mm. The phantom included 196 micro-channels of size 300 by 300 micrometers. The microchannels were cleaned using a WaterJet Objet using a 200 micrometer needle. Water was pumped through the phantom using a Masterflex Peristaltic pump. 3mm of Omnipaque contrast agent was administered using the Medrad Mark V contrast injector at a rate of 20 ml/sec. Digital subtraction angiography was used to image the phantom after the contrast was injected. Wood selected 3 flow rates of 250, 300, and 350 ml/min to use in the experiments. Exposure parameters were set to 80 kVp, 160 mA, SAD of 120 cm, 2 frames/sec, and FOV of 12.5 cm x 17.5 cm.

Wood developed a LabVIEW based software to derive time attenuation curves and calculate perfusion parameters from their imaging data. Wood calculated the maximum slope and area under the curve for each run. The system’s sensitivity was evaluated using the law of conservation of mass by comparing the total concentration in the arterial input and the venous output. To calculate the maximum slope, Wood took the maximum derivative value of the contrast as a function of time in the arterial input. To calculate the area under the time attenuation curve, Wood performed a numerical integration over the function. Wood also calculated the flow of the system using Fick’s law. The volume of the perfused area was determined by the physical size of the capillaries.

 The phantom was printed in high quality mode and was reproducible from print to print. The major problem associated with printing the phantom, was cleaning the support material out of the micro-channels. This required a large amount of time using a micro-needle to individually clean each hole. Wood was able to visualize the contrast uniformly moving throughout the capillaries for flow rates above 200 ml/min. In flow rates lower than this, the contrast agent would pool in the capillaries. The average value over the region of interest in the background of the acquired image was subtracted from the main regions of interest to minimize noise. The sensitivity of the system was exceptional as shown by the percent error of 1.15% between the difference in contrast of the arterial and venous output. This minimal error can be attributed to the inherent noise in the images. The constructed time attenuation curves were well behaved and accurately reflected the movement of the contrast bolus through the phantom. The maximum slope did increase with flow rate and the area under the curve decreased as would be expected. The percentage error between the calculated flow using Fick’s law and the actual measured flow was twenty five percent. Wood concluded that her phantom was reproducible and could be used to evaluate any commercially available CT perfusion system.

Overall, Wood was able to create a perfusion phantom that was physiologically relevant to the size of brain capillaries. Her design and method of manufacturing were simple and easily reproducible. The phantom was able to produce well-behaved time attenuation curves in the phantom with a very small error of system sensitivity of 1.5%. The drawbacks were that Wood did not do a very thorough quantitative analysis on her results. Her calculations of flow rates and areas under the curve did not show an absolutely linear correlation to input flow rates into the phantom as would have been expected. Her error on flow rate calculation using Fick’s law of twenty five percent was also exceptionally high. Wood also did not vary a wide range of parameters which could affect the shape of the time attenuation curve such as capillary diameter, and contrast concentration.

This paper proved to be a very useful to our study of CT perfusion. We decided to base our CAD design on the Wood phantom with minor adjustments. We included inserts for tubing at each end of the phantom, an O-ring for a watertight seal, and holes for screws to hold the phantom together. We also varied the length of the micro-channels as well as their diameter to obtain a wide range of time attenuation curve profiles. Larger capillary diameter also allowed for easier cleaning and possibly more accurate results. The 3D printer, peristaltic pump, and contrast injector that we decided to use are comparable or of higher quality than those used by Wood in this study. We also wrote our own processing algorithm to obtain time attenuation curves and perfusion parameters from the imaging data as part of the digital phantom component of the project. As an initial step to validate our phantom, we will perform similar testing to this paper. In summary, this paper provided us with an initial foray into perfusion imaging.

Wood, R. P., Khobragade, P., Ying, L., Snyder, K., Wack, D., Bednarek, D. R., … Ionita, C. N. (2015). Initial testing of a 3D printed perfusion phantom using digital subtraction angiography, *9417*, 94170V. <http://doi.org/10.1117/12.2081471>Her