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Group 4: CBCT Perfusion
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Seminar Paper: "Perfusion CT: a worthwhile enhancement?"

In this seminar we present the paper by Griffiths et al, "Perfusion CT: a worthwhile enhancement?" This was chosen from the reading list chiefly because it provides the clinical context and background necessary for our deliverables to eventually be useful to the relevant end users. In our project, "Cone Beam CT Brain Perfusion Sensing and Digital Simulators," we seek to develop reliable and physiologically realistic physical and digital phantoms which can be used to test the validity of perfusion imaging using C-arm Cone Beam CT (CBCT). This review paper highlights some of the important clinical applications of perfusion imaging, and describes the general concepts used in interpreting perfusion parameters. In addition, the paper also reviews the implementation issues faced in making perfusion imaging commercially available as well as in ensuring the methods may be validated in a reproducible manner. Although this assessment covers perfusion in a general sense, many of the themes are directly relevant to our project and will be used as a starting point during the testing and validation phases of our phantoms. Moreover, a general survey of the perfusion landscape will enable us to be aware of both the pearls and potential pitfalls of the technique while interpreting our results.

CT perfusion as a diagnostic tool began within several years after the advent of traditional CT. The general aim of these initial studies was to more precisely determine how

blood was distributed to the capillary bed within tissues, focusing on renal and myocardial flow in particular. However, with the development of advanced software packages as well as therapeutic options such as thrombolytics and anti-angiogenesis drugs, perfusion imaging is now being applied more generally. Today, the two prominent application areas are within acute stroke and oncology.

Acute stroke can be broadly divided into two types: ischemic and hemorrhagic. While hemorrhagic strokes present themselves through the rupture of key vasculature and can be detected on a conventional CT, they form a minority of cases. Due to the fact that up to 85% of strokes are actually ischemic in origin, CT measurements alone are not enough to conclusively perform the diagnosis. In ischemic stroke, the vasculature is actually obstructed due to the presence of some fatty deposits which line the interior of the vessel walls. While hemorrhagic stroke may be readily detected on the CT, ischemic stroke generally presents itself in a more subtle manner. Moreover, due to the limited time window for positive prognosis of about six hours, speedy and reliable evaluation is especially relevant. As a result, CT perfusion which can measure not only the amount of circulating blood, but also the transit time, cerebral flow, and cerebral volume is a promising option. Detection and localization of the stroke is important in tailoring the therapeutic options to best serve the patient. In the context of acute stroke, the clinician seeks to discriminate between the unrecoverable infarct tissues and the recoverable region known as the penumbra. In cases where the penumbra is greatly diminished for example, the risks may outweigh the benefits and administering treatment may introduce further complications to the patient. Due to such

factors, perfusion imaging can clarify the particular pathology and offers a critical step in aiding the decision making process.

To shed more light on the applicability of CT perfusion in acute stroke, we will go into some detail on stroke pathology and the physical intuition provided by the technique. To measure blood flow and related perfusion parameters, the perfusion is performed by injecting the patient with a non-ionic contrast bolus which circulates through the bloodstream within 20-30 seconds and subsequently imaged. In an ischemic stroke, cerebral blood flow will eventually witness a marked decrease from the 50 to 60 ml min^-1 100 g^-1 baseline. However, a relatively small drop in cerebral perfusion pressure can be accommodated through blood vessel dilation which serves to maintain the perfusion levels. While this compensatory mechanism makes discernment difficult in conventional CT, perfusion imaging can detect the increases in blood volume and transit times. As the perfusion levels drop to 20 60 ml min^-1 100 g^-1, the vasculature can be said to be reversibly damaged and identified as a potential penumbra region. While the ischemic stroke will eventually result in discernible decreases in perfusion, such cases often initially manifest through the mismatch between blood volume and perfusion. A recoverable penumbra indicates the vasodilation response is still working implying a corresponding increase in blood volume for the reduction in perfusion. However, a concomitant reduction in perfusion and blood volume is a red flag for an irrecoverable infarct.

From a technical viewpoint, perfusion imaging relies on the acquisition of repeated CT scans following the injection of the bolus contrast material. These scans allow for the construction of the related time-attenuation curves (TACs) which may be used to perform

further analysis. Among the numerous ways to quantify the TACs for perfusion parameters, the authors touch on the slope, deconvolution, and moments methods. While these methods differ in their technical approaches, they are all fundamentally rooted in linking the change in tissue perfusion to changes in the intensity of the CT following contrast enhancement. As such, these approaches involve a great deal of case by case analysis due to the variability of measurement and response among individual patients. While many of the theoretical ideas have seen commercial realizations such as the Siemens slope method implementation and the similar Philips perfusion package, the precision and reproducibility of the perfusion mapping is still in experimental stages.

In comparing the three methods of performing the perfusion: method of moments, slope, and deconvolution, the authors make some important points. In particular, they note that while the method of moments has been sufficiently validated using micro-spheres, the method may not be physiologically realistic and thus suffers in terms of accuracy when the conditions deviate from protocol. Moreover, while the slope method can calculate the perfusion parameters with much fewer sample frames than the deconvolution, it is more susceptible to the noise contained within individual samples. As such, the tradeoffs between time of acquisition and accuracy of the readouts need to be considered.

On the whole, the arguments made in this review are fair, assessing the field of CT perfusion imaging through a diverse range of clinical applications as well as technical approaches. However, while the article provides the gist of why and when CT perfusion should be implemented, there is not a great deal of guidance on how the studies should be conducted. In addition, the paper is somewhat inconclusive on precisely how reliable the

different methods of determining perfusion are when applied in different contexts. While this is understandable given the limited patient size and difficulty in controlling physiological perfusion parameters, some further direction would be desirable.

Our project is not directly considered with the physiological implications of different perfusion acquisition protocols and acquisition methods. Nevertheless, we desire to design and standardize a reliable protocol which may be used as a foundation for testing the phantoms. In this regard, our task is somewhat different from the review paper because we are also constrained by a limited sampling rate due to the hardware supported on the C-arm CBCT. While our problem is not precisely the same as the one tackled here, I believe many of the general principles of CT perfusion will be of great benefit in the next steps of evaluating our phantoms.

References:

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K A Miles and M R Griffiths
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