ROLE OF CT PERFUSION IN ADULT BRAIN TUMORS

(Diagnosis, grading and follow up)

Thesis

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DEDICATION

I would like to dedicate this thesis to my Father and my Mother; to them I will never find adequate words to express my gratitude.

Also my beloved wife and, for her continuous support and encouragement.

Finally tomy little son Marwan

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LIST OF ABBREVIATIONS

3D	Three dimensional
AUC	Area under the curve
BF	Blood Flow
BV	Blood Volume
CT	Computed tomography
KV	Kilo volt
Kg.	Kilograms
Lbs	Pounds
Ma	Milliamper
MDCT	Multi-detector computed tomogram
MIP	Maximum intensity projection
ml/min/100g	Milli-liters per minute per 100 grams
MTT	Mean Transit Time
mSv.	millisievert
NDL;	non diagnostic line
P+	The predictive value for a +ve test
P-	The predictive value for a -ve test
PS	Capillary permeability surface area product
PC	Personal computer
P value	Predictive value
ROI	Region of interest
SD	Standard deviation
SMV	Superior mesenteric vein
Sn.	Diagnostic Sensitivity
Sp.	Diagnostic Specificity
SPSS	Statistical package for social sciences
MVD	microvascular density

Introduction

Since its introduction by Godfrey Hounsfield in 1971, CT has largely been recognized as a powerful imaging tool for demonstrating internal anatomy. However, CT also has the ability to quantify physiological processes, as was first shown in 1980 when Axel published a methodology for the determination of cerebral blood flow by rapid-sequence CT. At that time, the speed of image acquisition and data processing of conventional CT systems was too slow for the technique to become widely accepted. ***(Padhani and Choyke 2006).***

The development of faster, spiral CT systems in the 1990s enabled the development of methodologies that could measure tissue perfusion and other physiological processes on conventional CT systems that were widely available. Interest in this area has been stimulated further, by the introduction of multislice CT and by the release of commercial perfusion CT software from a number of major equipment manufacturers. The first reported assessment of tumor physiology by conventional spiral CT was in 1993, which was a study of hepatic perfusion, including patients with metastases. ***(Padhani and Choyke 2006).***

Idea of CT perfusion

The main aspect of tumor biology that is accessible with CT is the physiology of the tumor vasculature. CT measurements of perfusion and other aspects of vascular physiology can therefore provide a noninvasive imaging marker for tumor angiogenesis in vivo. Angiogenesis has emerged as an important topic within oncology not only because tumors are dependent on vascularization for their ability to grow and metastasize, but also because angiogenesis is a potential target for anticancer therapeutic agents. ***(Padhani and Choyke 2006).***

To measure tumor perfusion with CT, contrast is injected intravenously, to 'label' the blood. Assuming that the injected contrast is uniformly mixed with blood, tracing blood through the tumor circulation is equivalent to tracking a bolus of contrast through the tumor ***(Miles and Cuenod 2007).***

The fundamental processes underlying CT measurement of tumor perfusion is the transport by blood flow of an intravenously administered iodinated contrast agent to the tumor and exchange by diffusion of these contrast molecules between the intravascular space and the extravascular interstitial space ***(Miles and Cuenod 2007).***

AIM OF THE WORK

The aim of this work is to evaluate the clinical application of CT perfusion as a non-invasive imaging tool in grading of adult brain tumor and evaluation of recurrence of tumor after surgical excision

Technical aspects of CT perfusion:

1) Physical aspects of CT perfusion:

CT can assess vascular physiology by measuring the temporal changes in X-ray attenuation that occur in major blood vessels and tissues after intravenous administration of conventional iodinated X-ray contrast agents. The measured increase in attenuation, quantified in Hounsfield units (HU), is proportional to the concentration of iodine. (**Padhani and Choyke 2006).**

2) Physiological Parameters measured by CT perfusion:

I. **Blood flow (BF):**This is the flow rate of blood within the vascular space in a tissue (e.g. tumor) region, expressed in units of milliliters per minute per 100 g of tissue. The blood flow measured with CT includes flow in large vessels, arterioles, capillaries, venules, and veins. **(Miles and Cuenod 2007).**

II. **Blood volume (BV):** This is the volume of blood actually flowing within the vascular space in a tissue region, expressed in milliliters per 100 g of tissue. Any stagnant pool of blood will not be included in the blood volume. It is measured in units of ml/100g **(Miles and Cuenod 2007).**

III. **Mean transit time (MTT):** This is the average time taken by blood elements to traverse the vasculature from the arterial end to the venous end in a tumor. If the perfusion pressure is high, blood elements are traveling at a higher velocity, resulting in a shorter mean transit time than when perfusion pressure is low. In this sense, mean transit time is a measure of perfusion pressure. Mean transit time is measured in seconds **(Miles and Cuenod 2007).**

IV. **Capillary permeability surface area product (PS):** it is the product of permeability and the total surface area of capillary endothelium in a unit mass of tumor (usually 100g), and hence is the total diffusional flux across all capillaries. It is measured in units of ml/min/100g. In other words, it is the unidirectional flux of contrast from blood plasma to interstitial space **(Miles and Cuenod 2007).**

3) <u>The protocol of performing CT brain perfusion study:</u>

The theory behind this technique is the central volume principle, which relatescerebralblood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) in the following equation: CBF-CBV/MTT.

Perfusion studies are obtained by monitoring thefirst pass of an iodinated contrast agent bolus through the cerebral

vasculature. There is alinear relationship between contrast agent concentration and attenuation, with the contrastagent causing a transient increase in attenuation proportional to the amount ofcontrast agent in a given region. (**Wintermark Met al, 2001).**

Contrastagent time-concentration curves are generatedin an arterial region of interest(ROI), a venous ROI, and in each pixel Deconvolution of arterial and tissue enhancementcurves (**Wintermark Met al, 2001).**

Perfusion CT scans are obtained at our study by using a multi–detector rowscanner (DUAL ENERGY 128 SIMENES). After unenhanced CT ofthe whole brain, four adjacent 5-mm-thicksections are selected starting at the level ofthe basal ganglia. At this level, all threesupratentorial vascular territories are visualized. (**Eastwood JDet al, 2001)**

Fifty milliliters of a nonionic contrastagent (300 mg of iodine per milliliter)is injected at a rate of 4 mL/sec. At 5 secondsafter initiation of the injection, a cine(continuous) scan is initiated with the followingtechnique: 80 kVp, 190–200 mA, 4-5-mm sections, 1-second per rotationfor a duration of 50 seconds. (**Eastwood JDet al, 2001)**

The scans are obtained at5 mm rather than 10 mm to lessen beamhardeningartifacts in the brain. The reformatted10-mm-