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# Diagnostic Accuracy of Perfusion CT in Grading of Gliomas

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## ABSTRACT

**Objectives:** To determine the diagnostic accuracy of perfusion CT in grading gliomas taking histopathology as gold standard. **Study design:** Cross-sectional validation study. **Setting:** Department of Radiology, Allied/DHQ Hospitals, Faisalabad. **Period:** Study was carried out over a period of six months from 01-09-2015 to 28-02-2016. **Methodology:** A total of 105 patients were included in this study. Low radiation dose non contrast CT head was performed to localize the region of interest before obtaining a perfusion scan. For the perfusion scan, 50ml of non ionic contrast is injected at a rate of 4-5ml/sec through an IV line by using an automatic power injector. At 5 seconds into the injection, a cine scan was initiated with the following technique: 80kv,100-120mA and 1 second/ rotation for a duration of 50 seconds. After the initial 50 sec cine scan, 8 more axial images were required, 1 image every 15 seconds for an additional two minutes, thus giving a total acquisition time of 170 sec to assess delayed permeability showing a large heterogeneous lesion with surrounding edema and mass effect on CT brain plain were included in the study. **Results:** Mean age of the patients was 49.4±16.1 year. There were 69 males (65.7%) and 36 females (34.3%). Comparison of perfusion CT findings versus histopathology in diagnosing high grade gliomas showed positive cases 77 and 95, respectively. Sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of perfusion CT was 78.9%, 80.0%, 79.0%, 97.4% and 28.6%, respectively. **Conclusion:** In conclusion, clinically available perfusion imaging tools by using CT can provide additional information regarding brain tumor vascular estimates, which could be useful imaging biomarkers for preoperative glioma grading and angiogenesis assessment and could also be useful for treatment planning and response assessment.

**Keywords:** Perfusion computer tomography, Brain gliomas, Diagnostic accuracy

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## INTRODUCTION

Gliomas, the most common primary brain neoplasms in adults are very heterogeneous tumors.[1] They arise from glial cells (astrocytes, oligodendrocytes).[2] Among the gliomas, astrocytic tumors are the most common and usually divided into circumscribed and diffuse forms. The circumscribed tumors are generally in lower grade occurring in young patients while the diffuse tumors are the most common cerebral tumors in adults belonging to WHO Grades II, III, IV.[3]

High grade gliomas can be highly invasive and extremely vascular tumors. Malignant brain tumors are characterized by neovascularity and increased angiogenic activity with a high proportion of immature and highly permeable blood vessels.[1] Overall the prognosis of high grade gliomas remain poor despite advances in diagnosis and therapy. The median survival is 12-15 months in patients of glioblastomas and 2-3 years in patients of anaplastic gliomas.[3]

Tumor grade differentiation is often difficult using routine neuroimaging alone. The recent technical developments have enabled a fast relatively simple, practical and available approach to assess essential parameters of vascular physiology namely regional cerebral blood volume (rCBV), regional cerebral blood flow (rCBF) and permeability surface area product (PS). CT perfusion imaging provides qualitative information on tumor vasculature that closely parallels the degree of tumor malignancy.[4,5]

The perfusion CT technique has been found to be useful in the evaluation of cerebral ischemia and infarctions but recent studies have investigated the role of perfusion maps for evaluating brain neoplasm's because there is growing interest in the non-invasive assessment of tumor vascularity.[6]

Quantification of tissue perfusion characteristics contributes to the production of tumor grade and plays an important role in prognosis, therapeutic management and treatment response.[7] Changes in PS and CBV values have good correlation with glioma grading with PS the best parameter correlating with glioma grade. Higher grade gliomas show higher PS and CBV as compared to low grade.[1] In one study in a group of 22 patients PCT detected 12 patients of gliomas (54.5%) and 10 patients of metastasis (45.5%).[6] The sensitivity and specificity of PS perfusion CT in grading gliomas is 70% and 88%.[8]

The aim of our study was to prove that perfusion CT is a non-invasive way of quantifying and classifying the characteristics of gliomas according to their regional perfusion parameters which will be helpful in early diagnosis and selection of appropriate treatment option by reducing the number of neurosurgeries.

## METHODOLOGY

**Study Design:** Cross-sectional validation study.

**Place of Study:** Department of Radiology, Allied/DHQ Hospitals, Faisalabad

**Duration of Study:** Study was carried out over a period of six months from 01-09-2015 to 28-02-2016.

**Methods:**

After taking approval from hospital ethical committee, a total number of 105 patients who range from 13-70 years of age of both genders were taken from radiology department referred by neurosurgeons that were showing a large heterogeneous lesion with surrounding edema and mass effect on CT brain plain and patients presenting with history of any of the following: headache, seizures, memory and visual loss, behavior change. Diagnosed cases of gliomas and other brain tumors were excluded from the study and the patients with history of epilepsy on EEG and patients allergic to IV contrast and with deranged RFTs. Non-Probability Consecutive Sampling technique was used for patient selection. Informed consent was taken and following procedure was started. Low radiation dose non-contrast CT head was performed to localize the region of interest before obtaining a perfusion scan. For the perfusion scan, 50ml of non-ionic contrast is injected at a rate of 4-5ml/sec through an IV line by using an automatic power injector. At 5 seconds into the injection, a cine scan was initiated with the following technique: 80kv, 100-120mA and 1 second/ rotation for a duration of 50 seconds. After the initial 50 sec cine scan, 8 more axial images were required, 1 image every 15 seconds for an additional two minutes, thus giving a total acquisition time of 170 sec to assess delayed permeability. ROI was drawn on contra lateral white matter as well. Maps of perfusion parameters was obtained by using the commercially available software applications. On perfusion CT gliomas show a cut off value of permeability surface area product (PS) of 3.6ml/100gm/min (≥3.6 identify high grade gliomas and<3.6 identify low grade glioma).

Perfusion CT result was confirmed by histopathology report collected from hospital pathology department and confirmed by consultant pathologist.

All data was analyzed by using SPSS version 16. Mean and standard deviation was calculated for age and PS. Frequency and percentage was calculated for all qualitative variables like gender and true positives. Sensitivity and specificity was calculated by constructing 2x2 table taking histopathology as gold standard. On histopathology high grade glial cells show increased cellularity, cellular atypia, endothelial proliferation and necrosis (presence of all).

| GLIOMAS ON HISTOPATHOLOGY | | | |
|---|---|---|---|
| High Grad Gliomas on Perfusion CT | | +VE | -VE |
| | +VE | a (TP) | B (FP) |
| | -VE | c (FN) | D (TN) |

Sensitivity= TP/TP+FN x 100
Specificity=TN/FP+TN x 100
PPV=TP/TP+FP x 100
NPV=TN/FN+TN x 100
Diagnostic Accuracy=TP+TN/TP+FP+FN+TN x 100

## RESULTS

A total of 105 patients were included in this study during the study period of six months from 01-09-2014 to 28-02-2015.

Regarding age distribution, majority of the patients were between 61-70 years old while minimum patients were 13-20 years of age. Mean age of the patients was 49.4±16.1 year (Table-1). There were 69 males (65.7%) and 36 females (34.3%) (Table 2).

Comparison of perfusion CT findings vERSUS histopathology in diagnosing high grade gliomas showed positive cases 77 and 95, respectively (Table-3).

Sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of perfusion CT was 78.9%, 80.0%, 79.0%, 97.4% and 28.6%, respectively (Tables 4 & 5).

**Table 1: Distribution of patients by age**

| Age (Year) | Number | Percentage |
|---|---|---|
| 13-20 | 07 | 6.7 |
| 20-40 | 23 | 21.9 |
| 41-60 | 35 | 33.3 |
| 61-70 | 40 | 38.1 |
| **Total** | **105** | **100.0** |
| **Mean** | **49.4±16.1** | |

**Table 2: Distribution of patients by gender**

| Gender | Number | Percentage |
|---|---|---|
| Male | 69 | 65.7 |
| Female | 36 | 34.3 |
| **Total** | **105** | **100.0** |

**Table 3: Comparison of Perfusion CT findings vs histopathology n = 105**

| High grade gliomas on Perfusion CT | High grade gliomas on Histopathology (Gold Standard) | | Total |
|---|---|---|---|
| | Positive | Negative | |
| **Positive** | 75 (TP) | 2 (FP) | 77 |
| **Negative** | 20 (FN) | 8 (TN) | 28 |
| **Total** | 95 | 10 | **105** |

**Key:**

TP = True positive
FP = False positive
FN = False negative
TN = True negative

**Table 4: Sensitivity, Specificity and diagnostic accuracy of perfusion CT**

$$\text{Sensitivity rate} = \frac{\text{True Positive}}{\text{True Positive + False Negative}} \times 100 = \frac{75}{75 + 20} \times 100 = 78.9\%$$

$$\text{Specificity rate} = \frac{\text{True Negative}}{\text{True Negative + False Positive}} \times 100 = \frac{8}{8 + 2} \times 100 = 80.0\%$$

$$\text{Diagnostic Accuracy} = \frac{\text{True Positive + True Negative}}{\text{True Positive + True Negative + False Positive + False Negative}} \times 100 = \frac{75 + 8}{75 + 8 + 2 + 20} \times 100 = 79.0\%$$

**Table 5: Positive predictive value and negative predictive value of perfusion CT**

$$\text{Positive Predictive Value} = \frac{\text{True Positive}}{\text{True Positive + False Positive}} \times 100 = \frac{75}{75 + 2} \times 100 = 97.4\%$$

$$\text{Negative Predictive Value} = \frac{\text{True Negative}}{\text{True Negative + False Negative}} \times 100 = \frac{8}{8 + 20} \times 100 = 28.6\%$$

## DISCUSSION

Computed tomography (CT) is a widely available and time-saving brain imaging method. It has a well established role as an examination of choice for imaging in an emergency setting. Over the last two decades computed tomography (CT) technology has undergone significant progress starting with multi section/spiral scanning and followed by expansion of multidetector CT (four to 128 detector-rows). These advances allowed quicker and more precise, three-dimensional (3D) acquisition, 3D CT angiography (CTA) and cerebral perfusion studies.[9]

Perfusion imaging delivers the information about regional differences of cerebral haemodynamics and can give additional information in different cerebral pathologies. The main values measured include cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT), the distribution of which can be presented visually as perfusion maps.

CT perfusion imaging with both structural and functional neuroimaging techniques has the growing potential to provide clinicians with more precise information in different cerebral pathologies.[9]

Gliomas are histologically very heterogeneous, with varying degrees of cellular and nuclear pleomorphism, mitotic activity, vascular proliferation, and necrosis.[10]

There are significant limitations associated with histopathologic grading, which include sampling errors[11] wide range of classification and grading systems used for brain tumors, inter- and intra-pathologist variability, and the changing nature of central nervous system tumors.[12] The degree of vascular proliferation is one of the most critical elements in the determination of tumor grade and prognosis, thus preoperative noninvasive assessment of glioma vascularity can be helpful in determining the malignant potential of the tumor, in selection of an appropriate biopsy site, in predicting transition from low-grade to a high-grade glioma, and also in monitoring response to various treatment modalities.[13]

Radiologic grading of tumors with conventional MR imaging is not always accurate, with sensitivity in identifying high-grade gliomas ranging from 55.1% to 83.3% in various studies.[14,15] Conventional MR imaging does not provide information on tumor physiology, which is also an important factor in determining the tumor grade.

Because angiogenesis is an important feature in malignant gliomas, perfusion imaging may provide additional important information. An overall principle of perfusion oncologic imaging is that with tumor growth, its metabolic demands increase due to rapid cell growth and cell turnover. Cellular hypoglycemia and hypoxia lead to the production of angiogenic cytokines, which leads to neoangiogenesis, which in turn increases the capillary attenuation within the tumor[16] increased capillary attenuation leads to higher blood volume and blood flow in the tumor bed.[16]

Perfusion computed tomography (PCT) shares the advantages of MR perfusion and potentially has advantages over MR perfusion because of easy accessibility, measurement of absolute perfusion values, and relatively easy post-processing. In addition, there are some important limitations associated with MR perfusion.

In present study, sensitivity, specificity, diagnostic accuracy, positive predictive value and negative predictive value of perfusion CT was 78.9%, 80.0%, 79.0%, 97.4% and 28.6%, respectively which is comparable with the Ramli et al.[8]

Limitations of our study includes: The technique is susceptibility-weighted. It is extremely sensitive to magnetic field inhomogeneity, and thus hemorrhagic products can complicate the analysis. Calculation of rCBV can be inaccurate in lesions such as GBM or meningioma, where there is a severe breakdown or absence of the blood-brain barrier.

## CONCLUSION

In conclusion, clinically available perfusion imaging tools by using CT can provide additional information regarding brain tumor vascular estimates, which could be useful imaging biomarkers for preoperative glioma grading and angiogenesis assessment and could also be useful for treatment planning and response assessment.

Because CT scanning is still much more easily available in most clinical facilities and much cheaper than MR imaging, its role is more and more linked with emergency cases.

PCT has the advantage of providing 2 of the most important tumor vascular estimates (ie, blood volume and permeability) in 1 single experiment as well as providing a linear relationship of tissue signal intensity with tissue contrast agent and the availability of an arterial input function unlike that in most of the available MR perfusion techniques; hence, PCT has the potential to be a useful tool for brain tumor assessment.

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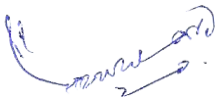
| **Dr. Hassan Bukhari**<br>Senior Registrar, Radiology<br>Allied Hospital, Faisalabad | Helped in the manuscript writing |  |
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