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ORIGINAL REPORT

The heterogeneity of blood flow on magnetic resonance imaging: A biomarker for grading cerebral astrocytomas☆

A.J. Revert Ventura[a,*], R. Sanz Requena[b], L. Martí-Bonmatí[b,c], Y. Pallardó[a], J. Jornet[d], C. Gaspar[e]

[a] *Servicio de Radiología, Hospital de Manises, Manises, Valencia, Spain*
[b] *Servicio de Radiología, Hospital Quirón Valencia, Valencia, Spain*
[c] *Servicio de Radiología, Hospital Universitario y Politécnico La Fe, Valencia, Spain*
[d] *Servicio de Radiología, Hospital de la Ribera, Alzira, Valencia, Spain*
[e] *Servicio de Oncología, Hospital de la Ribera, Alzira, Valencia, Spain*

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KEYWORDS
Astrocytoma;
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Abstract
Objectives: To study whether the histograms of quantitative parameters of perfusion in MRI obtained from tumor volume and peritumor volume make it possible to grade astrocytomas *in vivo*.
Materials and methods: We included 61 patients with histological diagnoses of grade II, III, or IV astrocytomas who underwent T2*-weighted perfusion MRI after intravenous contrast agent injection. We manually selected the tumor volume and peritumor volume and quantified the following perfusion parameters on a voxel-by-voxel basis: blood volume (BV), blood flow (BF), mean transit time (TTM), transfer constant (K^{trans}), washout coefficient, interstitial volume, and vascular volume.

For each volume, we obtained the corresponding histogram with its mean, standard deviation, and kurtosis (using the standard deviation and kurtosis as measures of heterogeneity) and we compared the differences in each parameter between different grades of tumor. We also calculated the mean and standard deviation of the highest 10% of values. Finally, we performed a multiparametric discriminant analysis to improve the classification.
Results: For tumor volume, we found statistically significant differences among the three grades of tumor for the means and standard deviations of BV, BF, and K^{trans}, both for the entire distribution and for the highest 10% of values. For the peritumor volume, we found no significant differences for any parameters. The discriminant analysis improved the classification slightly.
Conclusions: The quantification of the volume parameters of the entire region of the tumor with BV, BF, and K^{trans} is useful for grading astrocytomas. The heterogeneity represented by the

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* Corresponding author.
E-mail address: ajrevert@telefonica.net (A.J. Revert Ventura).

standard deviation of BF is the most reliable diagnostic parameter for distinguishing between low-grade and high-grade lesions.

PALABRAS CLAVE
Astrocitomas;
Resonancia magnética;
Perfusión;
Cerebro;
Tumores cerebrales;
Curtosis

La heterogeneidad del flujo sanguíneo en resonancia magnética, biomarcador para clasificar por grados los astrocitomas cerebrales

Resumen
Objetivos: Estudiar si los histogramas de los parámetros cuantitativos de perfusión por RM obtenidos a partir de los volúmenes tumoral y peritumoral permiten clasificar *in vivo* el grado de los astrocitomas.
Material y métodos: Se incluyen 61 pacientes diagnosticados histológicamente de astrocitoma grado II, III o IV, estudiados mediante RM de perfusión T2* con contraste intravenoso, seleccionando manualmente los volúmenes tumoral y peritumoral, cuantificándose vóxel a vóxel diferentes parámetros de perfusión: volumen sanguíneo (VS), flujo sanguíneo (FS), tiempo de tránsito medio (TTM), constante de transferencia (K^{trans}), coeficiente de lavado, volumen intersticial y volumen vascular.

Para cada volumen se obtuvo el histograma correspondiente con su media, desviación típica y curtosis, estas últimas como medidas de heterogeneidad, comparándose las diferencias por parámetro y grado tumoral. También se calcularon la media y desviación del 10% de los valores máximos. Finalmente se realizó un análisis discriminante multiparamétrico para mejorar la clasificación.
Resultados: En el volumen tumoral se obtuvieron diferencias estadísticamente significativas entre los 3 grados tumorales para la media y la desviación de VS, FS y K^{trans}, tanto para la distribución completa, como para el 10% máximo. En la región peritumoral no se obtuvieron diferencias significativas para ningún parámetro. El análisis discriminante mejoró ligeramente la clasificación.
Conclusiones: La cuantificación de parámetros del volumen total de la región tumoral con VS, FS y K^{trans} es útil para establecer el grado de los astrocitomas. La heterogeneidad, representada por la desviación típica del FS, es el parámetro con mayor fiabilidad diagnóstica para separar los tumores de bajo y alto grado.

Introduction

From the histological viewpoint astrocytomas are heterogeneous neoplasms in which in the same tumor both low- and high-grade areas coexist the latter being the ones that define the true histological differentiation.[1] Vascular proliferation is one of the histopathological descriptors used to categorize glial tumors.[1] These neoformed vessels show anomalies during their development, maturation and distribution within the neoplastic tissue and the surrounding peritumoral region. On the other hand they have an infiltrating nature enabling the coexistence of both healthy and tumor tissues in the surrounding brain tissue. This is why with the help of perfusion studies using magnetic resonance images (MRI) and spectroscopy with MRI the characteristics of peritumoral area have been used to distinguish between glial and metastatic lesions.[2–4]

Perfusion studies using MRI give us information on how angiogenesis and patency can alter the tumor vessels. As a matter of fact the parameters derived from the quantitative analysis of perfusion help us categorize tumor degrees in a much better way than conventional MRI–based on morphological criteria only.[5,6]

The quantitative analysis of perfusion uses a monocompartmental mathematical model assuming that the contrast media remains in the intravascular space and is not extravasated into the interstitial media. From that model the tissue values of blood volume (BV), mean transit time (MTT) and blood flow (BF) can be obtained usually as a measure on the healthy white matter.[7,8] Since tumors are dysfunctional when it comes to the patency of the hematoencephalic barrier (HEB) with extravasation of the contrast media from the vascular to the interstitial compartment, a 2-compartment model is used to measure the transfer dynamics of contrast media by using the transfer coefficient (K^{trans}), the vascular (v_p) and interstitial volumes (v_e) and the cleanser coefficient (k_{ep}).[9] Several studies have shown that there is a good correlation between the BV and the tumor stage of astrocytomas which allows us to distinguish between medium-grade (II) and high-grade astrocytomas (III and IV).[5,6,10–13] The relation between K^{trans} and the tumor stage is more controversial.[14,15]

Even though the data from perfusion studies using MRI are usually analyzed using average values from the regions of interest (ROI) a more accurate way to evaluate changes is to analyze the histogram of ROI or of the whole tumor