INTRODUCTION
Malignant gliomas of the brain are observed in 40% of patients from the total number of patients with brain tumors [1, 2].

The main method for the treatment of gliomas remains surgical resection of tumor tissue, total or subtotal, depending on the location, size and extent of the tumor. In some cases, when the glioma is localized in the brain, in the stem, subcortical, or middlebrain structures of the brain, surgery is associated with a high risk, and in these cases it is advisable to perform a stereotactic biopsy to establish an accurate histological diagnosis, followed by radiotherapy and/or stereotactic radiosurgery [3, 4].

Stereotactic radiosurgery can be used either as a single treatment method or in combination with whole brain radiotherapy (WBRT) and chemotherapy [5, 6, 7].

Postradiation changes after stereotactic radiosurgery (SRS) is often difficult to distinguish from local tumor progression [8, 9]. In the case of local recurrence of a tumor after radiosurgical treatment, in the event that surgical resection is not possible, the next stage of treatment can be considered as repeated radiosurgery (single or for several fractions) or irradiation of the entire brain, depending on the size and extent of the process [10].

In case of confirmation of post-radiation changes, further MRI observation and symptomatic therapy are recommended, except in cases where pronounced signs of the mass effect, dislocation syndrome and the clinical condition of the patient require urgent surgical intervention.

Of the non-invasive methods for the differential diagnosis of local tumor recurrence and necrosis, SPECT (sin-
gle-photon emission computed tomography), MR-spectroscopy and PET are used. In addition to the financial and labor-intensive aspects of these methods, one of their main drawbacks is that relatively low resolution methods may not allow early detection of tumor recurrence, while MRI perfusion methods have higher spatial resolution and demonstrate better results in the differential diagnosis of radionecrosis and recurrence of metastatic lesions [11,12].

Non-contrast MRI perfusion data based on arterial spin labelling (PASL) can quantitatively and qualitatively determine the density of blood supply and the relative regional blood flow in the tumor focus and in rrCBF and can be used for differential diagnosis of radionecrosis and tumor recurrence, followed by histological confirmation of the diagnosis [13-14]. However, in the literature, there are few data on the use of non-invasive contrast-free MRI perfusion based on arterial spin labelling (PASL) to determine the recurrence of brain metastases after stereotactic radiosurgery [15].

THE AIM
The aim of our study was to assess the possibility of non-invasive contrastless MRI perfusion based on arterial spin labelling (PASL) in the differential diagnosis of radionecrosis and local tumor recurrence in patients with brain metastases after stereotactic radiosurgery.

MATERIALS AND METHODS
We carried out a retrospective analysis of perfusion data based on PASL in 20 patients diagnosed with malignant brain glioma, who were treated using the stereotactic radiosurgery in one or more fractions and in which they underwent differential diagnosis of local recurrence (LR) and radionecrosis (RN). Of the total number of patients, there were 13 men and 7 women. The average age of 44 years.

The diagnosis of Malignant Brain Glioma (MBG) before stereotactic radiosurgery was established on the basis of a histological study using stereotactic biopsy data. Anaplastic astrocytoma (AnAST, grade III) was diagnosed in 6 patients and glioblastoma (GBM, grade IV) in 14 patients.

The average tumor volume was 4.0 cm³. The average dose of radiation was 15 Gr (in the range from 12 to 22 Gr), depending on the volume and location of the tumor.

After stereotactic radiosurgery, in addition to standard MRI methods, after 1.5 months, 3 and 6 months, the patients underwent non-invasive MRI perfusion based on arterial spin labelling (PASL).

MRI scan was performed on the “Intera” device (Philips, the Netherlands). The following sequences were used: fast-spin-echo-axial T2WI, spin-echo-axial T1WI, FLAIR, PASL and axial contrast and coronary T1WI.

PASL perfusion of MR images, carried out with the use of multisection sensitive streams with alternative inversion-recovery (FAIR). The FAIR sequence used variable selective and non-selective pulse-inversion (RF) pulses and was performed during TI 1200 ms between marking and image acquisition.

We selected the T1 range from 800 to 1600 ms based on the T1 decay of the magnetically-labeled water protons. That is, final FAIR perfusion maps were obtained by subtracting non-selective “inversion-recovery” images from selective images. When conducting the technique of multisection FAIR, we used the image parameters: TR / TE, 2000/15 ms; FOV 24 cm; matrix size 128 × 128; NEX 100; profile thickness, 5 mm; section number, 7; and section gap, 2 mm.

To calculate the diagnostic parameters of PASL, we used a qualitative evaluation system based on the intensity of the tumor signal by perfusion. We analyzed the zones of interest and calculated the ratio of the signal intensity with the maximum and average tumor perfusion (rTPmax and rTPmean). MRI data were evaluated, both quantitatively and qualitatively.

Quantitative analysis of the perfusion data was determined by the rrCBF values in the brain tumor tissue and the tissue of the normal medulla of the opposite hemisphere of the brain. The measurements were carried out in 6 pixels of the gray and white matter of the contralateral hemisphere. At the same time, measurements in the zone of peritumoral edema, necrosis and hemorrhages were avoided. According to the results of research, rrCBF compiled PASL cards. The rrCBF values in healthy brain tissue were calculated with respect to the white and gray matter blood flow (WM / GM) and blood flow to metastasis tissue, in relation to the gray matter of the contralateral hemisphere of the brain (MTS / GM). Accurate quantification of the PASL sequence depended on arterial transit time and local tissue and blood relaxation time, regardless of vessel size and oxygenation.

Statistical analysis was performed using IBM SPSS Statistics Version 20 software. Licensed Materials – Property of IBM Corp.

RESULTS AND DISCUSSION
In total, perfusion data from 20 patients were evaluated according to PASL. In our study, the diagnosis of local tumor recurrence according to the relative regional blood flow based on PASL was confirmed in all 8 cases (Fig. 1).

Radionecrosis was diagnosed in 12 cases and was also confirmed in all cases. An example of clarity can be the case when, according to rrCBF PASL data, rTPmean and rTPmax indicators, changes in the glioblastoma focus after stereotactic radiosurgery were considered as a manifestation of radionecrosis, which was subsequently confirmed according to the navigation biopsy data.

CT perfusion data demonstrate multiple hyperperfusion sites that do not distinguish tumor recurrence sites from radionecrosis sites, due to postradiation disorders of the vessel wall permeability, pulse arterial spin labelling (PASL) allows for accurate differentiation of tumor recurrence (white curved arrow), confirmed by biopsy.

Radiation necrosis was subsequently removed surgically, as it behaved volumetrically and caused dislocation of brain structures. According to the histological conclusion in the obtained material, areas of coagulation necrosis were determined, with no “live” tumor tissue in the material (Fig. 2.1. and 2.2.).
Using the PASL cards, a suspicious area was found for the presence of “live” tumor tissue with angiogenesis (arrow), however, rTPmax 1.2 and rTPmean values of 0.7 ml / 100 g/min indicated radionecrosis. According to the PASL maps, a navigation biopsy was performed to obtain biopuncture, then the lesion with the cyst was resected. The histological conclusion confirmed the presence of a post-radiation focus of coagulation necrosis with a cyst, with no signs of tumor recurrence. According to MRI postcontrast T1WI before SRS (A) and after 6 weeks (B), the lesion increased in volume by 5 cm³. According to PASL perfusion after 6 weeks (C), rrCBF
values increased to 1.64 (compared to baseline 1.35 ml / 100g/min to stereotactic radiosurgery) and after 6 months to 1.85ml / 100g / min., the image with PASL overlay on T1WI (D). According to rrCBF PASL, there is a progression of the disease in the area of brain lining. Surgical resection was performed. The diagnosis of relapse is confirmed on the basis of histological examination.

In general, according to our data, the average rrCBF based on arterial spin labelling (PASL) rTPmean≤ 0.8ml / 100g / min most likely was in favor of radionecrosis, the average figure ≥ 1.5ml / 100g / min – in favor of tumor progression, the maximum rTPmax ≤ 1.3ml / 100g / min most likely testified in favor of radionecrosis, the maximum rTPmax> 1.8ml / 100g / min – in favor of tumor progression (Table 1).

When considering subgroups of patients with a histologically confirmed diagnosis or with spontaneous regression of a tumor, our data showed high sensitivity and especially specificity (up to 100%), most significant for the progression of the process with rrCBF mean MTS / GM> 1.5ml / 100g / min, with a sensitivity of 96.6%, specificity of 100% and accuracy of 98.4% (Table 2).

In our observations, PASL perfusion demonstrated significant and reliable indicators of differentiation of radionecrosis with a rrCBF index of <0.8mlml / 100g / min and a sensitivity of 85.5%, a specificity of 100% and an accuracy of 96.2% (p = 0.002), and a local tumor recurrence indicator of rrCBF> 1.5 ml / 100g / min and sensitivity 96.6%, 9 specificity 100% and accuracy 98.4% (p = <0.001), which is similar to literature data [10, 14,15].

CONCLUSIONS
These non-invasive PASL perfusion techniques that determine the relative regional blood flow of rrCBF are sufficiently informative and accurate in the differential diagnosis of radionecrosis and local tumor recurrence in patients undergoing radiosurgery for malignant gliomas of the brain.

REFERENCES

Table 1. Regression Logistic Analysis Result

<table>
<thead>
<tr>
<th>PASL performance</th>
<th>radionecrosis (n=24)</th>
<th>relapse (n=8)</th>
<th>Confidence indicator 95%</th>
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<tr>
<td>rTPmean</td>
<td>0.8ml/100gr/min</td>
<td>1.5ml/100gr/min</td>
<td>0.002 (-3.96-1.01)</td>
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<tr>
<td>rTPmax</td>
<td>1.3ml/100gr/min</td>
<td>1.8ml/100gr/min</td>
<td>&lt;0.001 (-2.36-0.84)</td>
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Table 2. Indicators of sensitivity, specificity and accuracy according to rrCBF PASL

<table>
<thead>
<tr>
<th>Indicators PASL</th>
<th>X²*</th>
<th>Credibility</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Accuracy (%)</th>
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<tbody>
<tr>
<td>rrCBF map</td>
<td>10.329</td>
<td>&lt;0.001</td>
<td>86.8</td>
<td>100</td>
<td>96.6</td>
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<tr>
<td>rrCBF MTS/GM</td>
<td>6.528</td>
<td>&lt;0.001</td>
<td>83.3</td>
<td>100</td>
<td>94.2</td>
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<tr>
<td>rCBFmean MTS/GM &lt; 0.8</td>
<td>8.764</td>
<td>0.002</td>
<td>85.5</td>
<td>100</td>
<td>96.2</td>
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<tr>
<td>rCBFmean MTS/GM &gt;1.5</td>
<td>19.538</td>
<td>&lt;0.001</td>
<td>96.6</td>
<td>100</td>
<td>98.4</td>
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ORCID and contributionship:
Andrey B. Gryazov: 0000-0003-1785-6705 \(^{A, D, C, D, E, F}\)
Yulia W. Medvedovskaya: 0000-0001-5119-0316 \(^{A, D, C, D, E, F}\)
Andrey A. Gryazov: 0000-0002-2210-1430 \(^{A, D, C, D, E, F}\)

Conflict of interest:
The Authors declare no conflict of interest.

CORRESPONDING AUTHOR
Yulia W. Medvedovskaya
Institute Of Neurosurgery Of The Academician
A.P. Romodanov Of Namn Of Ukraine
32 Platon Mayboroda st., 04050 Kyev, Ukraine
tel: 066-100-48-94
e-mail: medvedovsky@ukr.net

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\(^{A}\) — Work concept and design, \(^{B}\) — Data collection and analysis, \(^{C}\) — Responsibility for statistical analysis,
\(^{D}\) — Writing the article, \(^{E}\) — Critical review, \(^{F}\) — Final approval of the article