challenging. Tissue characterization, identification of important features for surgical planning, and prognostic biomarkers individuation can be enhanced by the use of advanced imaging techniques.

Spectroscopy

Spectroscopy is an MRI technique used to assess metabolite concentration in a region of interest. Therefore, it can be used for differential diagnosis both to differentiate between intra- and extra-axial masses and to exclude the hypothesis of dural metastases in the case of extra-axial dural-based mass in oncologic patients. Meningiomas show elevated choline and decreased N-acetylaspartate as well as decreased creatinine, a metabolic profile common to other neoplastic processes and therefore quite unspecific; conversely, increased alanine has demonstrated to be specific for meningioma but can be difficult to identify[32,33]. An elevated metabolite peak at 3.8 parts per million has been described in meningiomas, allowing to differentiate them from high-grade gliomas and intracranial metastasis. MR spectroscopy has been demonstrated to not be able to differentiate atypical meningiomas from typical ones[34,35]. Lactate peak is considered suggestive of aggressiveness, but it can also be found in benign meningiomas. Nevertheless, lactate and macromolecular peaks have demonstrated significant differences in meningothelial, fibrous, and oncocytic subtypes, showing the potential to characterize various lesion components[36].

Perfusion imaging

MR perfusion is a technique used to assess blood flow in tissues and includes the dynamic susceptibility contrast (DSC) technique and the dynamic contrast enhancement (DCE) technique, both requiring the administration of intravenous gadolinium, and arterial spin labeling. Meningiomas are highly vascular lesions, deriving their blood supply from meningeal arteries and consequently demonstrating very high perfusion. The complete lack of the blood-brain barrier determines increased contrast leakage and permeability, represented by a typical time-intensity curve: rapid drop during the first pass of contrast and slow return to a level lower than brain parenchyma[37]. MR perfusion can be useful in differential diagnosis, in particular to differentiate meningiomas from dural-based metastases and from high-grade gliomas invading the dura mater. Indeed, MR perfusion may differentiate between meningioma and dural metastases from various origins (breast, colon, and prostate) but not from hypervascular metastases, such as those from melanoma, renal carcinoma, or Merkel cell carcinoma (increased cerebral blood volume)[38]. The assessment of the time-intensity curve can distinguish a primary glial neoplastic process from intracranial metastases/meningiomas: in the former, the curve shows more than 50% return to baseline, while, in the latter, the curve shows less than 50% return to baseline due to breakdown in blood-brain barrier and dural-based blood supply. Meningioma vascularity appears to be significantly related to cerebral blood flow (CBF) values[39-41] and lately a significant correlation between CBV and expression of vascular endothelial growth factor has also been demonstrated, suggesting the possibility to use perfusion MR to predict refractoriness to conventional treatment and possible responsiveness to anti-angiogenic therapies. Correlation between relative CBV (rCBV) and Ki67 proliferative index has also been demonstrated in meningiomas but several studies have shown contrasting results about a possible correlation between tumoral perfusion parameters and meningioma grade, probably because of increased vascular permeability of meningiomas, due to lack of blood-brain barrier[22,42,43]. On the contrary, peritumoral rCBV has shown a potential diagnostic role: although peritumoral rCBV usually shows decreased values in meningiomas, possibly due to peritumoral vasogenic edema[44], its values are higher in the case of anaplastic meningiomas (WHO Grade III) compared with the other types[45]. Similarly, decreased peritumoral CBF can be measured with CT perfusion, potentially representing ischemic tissue salvageable after meningioma resection[46]. Arterial spine labeling has the advantage of assessing perfusion without the confounding permeability influence, potentially allowing to differentiate WHO Grade I from WHO Grades II and III intracranial meningiomas[47]. Vascular permeability represents another measurable parameter, assessed directly via DCE technique and contributing to meningioma grading: atypical meningiomas have shown higher values of Ktrans compared with benign meningiomas[48]. MR perfusion can be helpful also in distinguishing some

meningioma subtypes. In particular, angiomatous meningioma has demonstrated higher tumor rCBV compared with meningothelial, fibrous, or anaplastic subtypes[45].

Diffusion tensor imaging

Given the possibility to assess magnitude and directionality of water diffusion, diffusion tensor imaging (DTI) has been applied to differentiate meningioma grades. Although in most studies high-grade meningiomas have demonstrated low ADC values when compared with low-grade ones, controversial results have been obtained especially for the other DTI parameters[49-51]. DTI has shown promising potential in terms of preoperative consistency prediction. Besides some contrasting findings, most studies have shown higher fractional anisotropy (FA) values in hard meningiomas compared to soft ones[52-54]. Signal intensity on FA and mean diffusivity maps have also been found to be predictive of meningioma consistency[52,53,55]. Tractography, derived from DTI data, may give additional information for treatment planning of skull base meningiomas, but it is usually not necessary: resolving the course of cranial nerves with CSF sensitive sequences is technically easier and less sensitive to artifacts[12].

MR elastography

MR elastography (MRe) is a promising emerging technique that may have the potential to define tumor consistency and its relationship with adjacent structures. It provides a measurement of tissue stiffness, determined by the assessment of share wave movement through that given tissue. Recent studies have demonstrated a significant correlation between the MRe measurements and intraoperative qualitative assessment of tumor consistency[33]. Furthermore, differing stiffness on both sides of a tissue boundary allow defining the measurement of freedom of the adjacent tissue planes, thus evaluating the marginal invasiveness[56].

Molecular imaging

The most used molecular imaging technique in oncological field is 2-$^{[18F]}$-fluoro-2-deoxy-D-glucose (18F-FDG)-PET, which uses a glucose analog to identify metabolically active cells, but it does not have a primary role in intracranial tumors diagnosis due to high physiological FDG uptake in cerebral cortex and FDG accumulation in inflammatory processes. The ability of FDG-PET to differentiate meningioma grades has shown contrasting results. Although some studies have demonstrated its ability to differentiate benign meningioma from atypical/malignant ones and to distinguish recurrent/growing meningiomas from static ones, there is a lack of correlation between FDG uptake and WHO grading, MIB-1 labeling index, and tumor doubling time[12]. On the other hand, a high meningioma-to-background contrast can be obtained using radiolabeled somatostatin receptors II (SSTR II) ligands due to the increased expression of SSTR II in meningiomas compared to the very low expression in bone and brain tissue[57,58]. PET with gallium-68-labeled SSTR-ligands, such as 68Ga-DOTATOC (DOTA-(Tyr3)-octreotid) and 68Ga DOTATATE (DOTA-DPhe1-Tyr3-octreotate), has demonstrated a higher sensitivity in detecting meningiomas when compared to contrast enhanced MRI[59]. SSTR-PET is also useful for differential diagnosis, for example when studying optic sheath meningioma[60]. This technique also allows a detailed meningioma extent delineation, necessary for treatment planning but challenging in the case of complex localization (skull base, orbit, falx cerebri, sagittal, and cavernous sinuses), trans-osseous growth, or in pre-treated meningiomas, when MR contrast results are limited[12,61]. Integration of SSTR-PET imaging increases the precision of resection and target radiation. Furthermore, SSTR-PET can differentiate viable tumor and scar tissue using a semi-qua ntitative data analysis, since semi-quantitative uptake values (SUV) correlate significantly with SSTR II expression assessed by immunostaining. Patient treatment stratification can take advantage of SSTR-PET since SUV measurements have also demonstrated a correlation with tumor growth rate in WHO Grades I and II meningiomas (not in Grade III). Furthermore, SSTR-PET has been demonstrated to be more specific for detecting residual meningioma and may be considered in the case of equivocal MRI findings[62-64]. Recently, the RANO-PET taskforce has proposed an evidence-based recommendation for the use of

molecular imaging in meningiomas, even if the utility of SSTR II imaging needs more validation to be confirmed[65].

FUTURE DIRECTIONS

Radiomics is an emerging field of research that extracts many features from medical images. There are two categories of features, which can be extracted from the region of interest after the lesion segmentation, semantic and agnostic ones. In detail, semantic features are commonly used in the radiology lexicon to describe a lesion (e.g., shape, location, *etc*.), but in the radiomics field they are quantified through computer assistance. On the other hand, diagnostic features describe lesion heterogeneity using quantitative descriptors. They include first-, second-, or higher-order statistics. First-order statistical outputs consist of the grey level histogram analysis of the lesion's voxels. Second-order statistics are those obtained from texture analysis. They describe relationships between voxels considering their contrast values. Finally, higher-order statistics are obtained imposing filters to extract definite image patterns, such as fractal analyses, wavelets, or Laplacian transforms of Gaussian bandpass filters[66]. Radiomics can be coupled with artificial intelligence, which employs algorithms to allow computers to learn directly from the data and make predictions on unseen datasets, because of its better capability of managing this volume of data compared to traditional statistics[67]. In the study of meningiomas, radiomics and artificial intelligence have shown promise in preoperative evaluation, recurrence and outcome prediction, and radiation treatment planning. Preoperative prediction of the meningioma grade is important because it influences the treatment strategy. Park *et al*.[68] obtained an accuracy of 89.7% for the prediction of meningioma grades using MR conventional and diffusion tensor imaging with a radiomics and machine learning approach; furthermore, various texture parameters differed significantly between fibroblastic and non-fibroblastic benign meningiomas. Volumetric assessment of meningiomas is also highly relevant for therapy planning and monitoring. Using a multiparametric deep-learning model on routine MRI data, Laukamp *et al*.[69] investigated its performance in automated detection and segmentation of meningiomas in comparison to manual segmentations, obtaining a strong correlation despite diverse scanner data. Moreover, prognostic models based on clinical, radiologic, and radiomic feature have been investigated to preoperatively identify meningiomas at risk for poor outcomes. In this setting, preoperative radiologic and radiomic features such as apparent diffusion coefficient and sphericity have proved effective in predicting local failure and overall survival in these patients[70]. MR radiomics has also been implemented to predict early progression or recurrence, which characterize a subset of skull base meningiomas, achieving good results (accuracy 90%)[71]. Finally, radiomics has proved useful in the definition of radiotherapy target volume, which represents a critical step in treatment planning, in order to improve the texture-based differentiation of tumor from edema and to differentiate vasogenic from tumor cell infiltration edema[72].

CONCLUSION

Although generally easily identified on the basis of some pictorial neuroimaging features, meningiomas can raise some concerns in terms of tissue characterization and treatment selection. In particular, surgery largely relies on MRI and CT scans examination, as the type of therapeutic approach can vary depending on tumor size and location. Modern imaging tools are helpful in identifying more aggressive histological behavior, defining vessel and brain involvement, and evaluating the need for adjuvant therapies; at the same time, emerging post-processing techniques can enhance tumor biology tracking and response to therapy prediction. All these imaging-derived data coupled together may allow for optimal therapeutic planning and tailored longitudinal follow-up, based on both patient and tumor fingerprinting.

DECLARATIONS

Authors' contributions

Made substantial contributions according to ICMJE criteria: Elefante A, Russo C, Di Stasi M, Vola E, Ugga L, Tortora F, De Divitiis O

Conception and design: Elefante A

Writing: Russo C, Di Stasi M, Vola E, Ugga L
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