2 When and How to Use Imaging in Brain Tumors, Protocols

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2.1 Introduction

Modern imaging techniques are the primary means of diagnosis of brain tumors [1]. They are also used to decide on best treatment options based on possible tumor grade, plan biopsy and surgery, evaluate extent of tumor resection, assess response to treatment, and detect recurrence.

This chapter will provide an overview of when to use imaging for brain tumors, a general overview of follow-up imaging, criteria used to assess treatment response, and recommended protocols. While the use of advanced imaging methods will be mentioned and some aspects of conventional MRI sequences will be discussed, these will be in the context of their utility in general terms. Details regarding specific uses, pearls and pitfalls of conventional sequences, and advanced imaging techniques will be discussed in other chapters of the book.

2.2 When to Use Imaging

2.2.1 Diagnosis

MRI remains the cornerstone of brain tumor imaging, and is considered the standard imaging method for diagnosis [2]. In cases where a brain tumor might be suspected, such as those with chronic headache with new features or increasing frequency, new onset headache with optic disc edema, nontraumatic seizure in patients older than 40 or with focal neurologic deficit, the most appropriate imaging is MRI with and without contrast [3, 4]. CT can be used in the emergency setting, or to look for calcification in selected patients.

While a specific histopathological diagnosis may not be possible based on the images, it is usually not needed. In many cases the distinction of low- and high-grade lesions is more important, and many patients will have biopsies or surgery for histopathologic diagnosis and molecular studies (and in case of surgery, for treatment) in any case.

2.2.2 Preoperative Planning

Surgery remains the cornerstone of treatment of brain tumors and maximum safe resection is recommended in all patients with newly diagnosed gliomas whenever feasible [2]. While some tumors in eloquent cortex or brainstem have been traditionally considered inoperable, recent advances in neurosurgery and mapping techniques make it possible to operate on at least some of those lesions [5].

In certain cases, biopsy may be preferred before (or instead of) surgery. It is well known

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Y. Özsunar, U. Şenol (eds.), *Atlas of Clinical Cases on Brain Tumor Imaging*,
https://doi.org/10.1007/978-3-030-23273-3_2

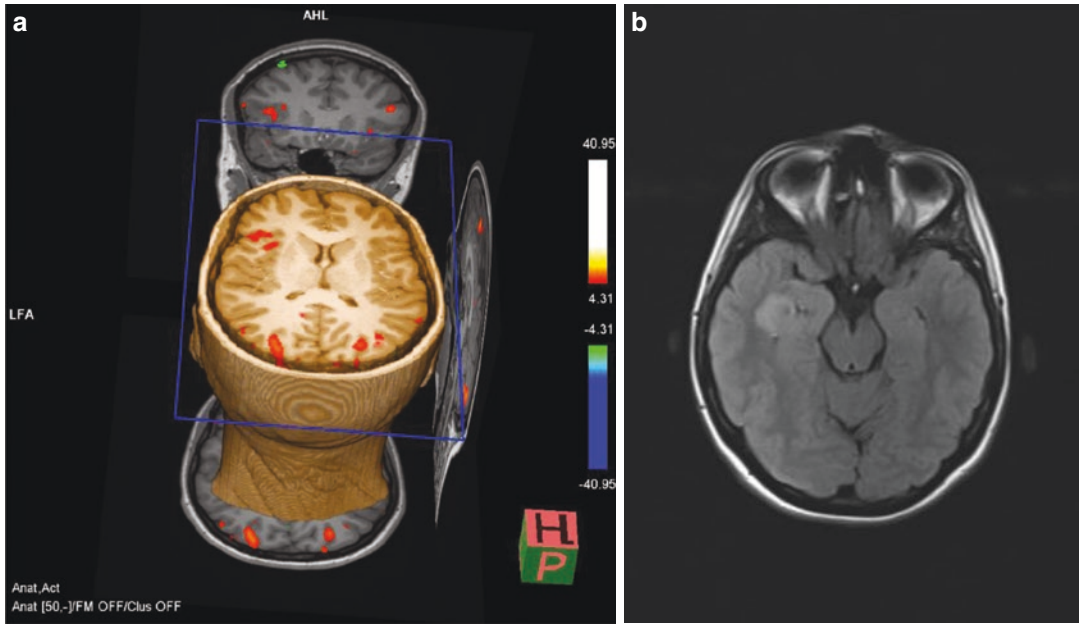

Fig. 2.1 fMRI study (**a**) to determine the location of the Broca area and plan surgery accordingly in a patient with a right temporal mass (**b**). The Broca region is demonstrated to be on the left side, which would have been impossible to determine with conventional MRI

that the heterogeneity of gliomas can cause undergrading and misdiagnosis due to sampling errors in biopsy [6]. In such patients, advanced imaging techniques can be used to target specific regions of interest to potentially improve diagnostic accuracy [6, 7].

MRI is also used in preoperative planning for navigational purposes. This is usually done with contrast-enhanced 3D-SPGR sequences that allow for high resolution and easy distinction of the tumor due to contrast enhancement. Coupled with some fiducials placed on the patient's head before the imaging study, these images can be used for intraoperative navigation. Imaging with head frames can also be performed for the same purpose in stereotactic radiosurgery or frame-based stereotactic biopsy.

Another factor with potential impact on surgery is the relation of the lesion to eloquent brain and critical white matter tracts [8]. Conventional anatomic MR imaging is insufficient to provide this information; for instance, while one can easily tell if a lesion is in the motor cortex provided one knows where the motor cortex is in that patient; brain mapping is not generalizable and must be done in a patient specific manner [9]. Functional MRI can be used to evaluate the location of the lesion with respect to eloquent brain (Fig. 2.1). The relationship of white matter tracts with the tumor can be delineated using diffusion tensor imaging (DTI) [8, 10]; thus DTI can also help improve tumor resection [11] and reduce the risk of new postoperative neurological deficits [12].

2.2.3 Intraoperative Imaging

Intraoperative MRI (iMRI) scans are beginning to get more widespread. The extent of resection is one of the factors improving overall survival in patients with gliomas [13] and use of intraoperative imaging makes it easier to ensure that as much of the lesion as is surgically feasible has been taken out [2]. This allows immediate further resection in the same session [14] and improved overall survival and progression-free survival have been reported by some groups [15, 16]. Despite these apparent benefits, there is a high cost of installation and an increase in the

healthcare cost and length of surgery [13]. There are also few studies providing high-quality evidence and evaluating whether the use of iMRI translates to improved progression-free survival or overall survival [14].

2.2.4 Postoperative Imaging

In the immediate postoperative period, unless there are operative complications or clinical concern, imaging is usually performed to determine the extent of tumor resection. In this situation, MRI is the modality of choice, provided the patient is clinically stable and there are no contraindications to an MRI scan.

Post-op imaging is also required to act as a baseline for further follow-up. The most appropriate time for baseline imaging to evaluate residual tumor is considered to be within 24–48 h of surgery and no later than 72 h [2, 17, 18]. Diffusion-weighted imaging (DWI) can also be included in the baseline imaging to determine if any future enhancement would be due to recurrence or ischemia related to surgery [18]. However, it should be noted that RANO criteria for diffuse low-grade gliomas recommend the baseline postoperative images to be preferably acquired 2–3 months after the surgery to minimize the effects of postsurgical changes such as edema, ischemia and enhancement and to better evaluate the extent of resection of non-enhancing tumors [19].

2.2.5 Follow-Up Imaging

There are two different scenarios where follow-up imaging is performed: To follow up the lesion after treatment for recurrence or progression of any non-resected parts of the mass; and to follow up lesions that did not receive any treatment. While the imaging protocol is similar in both cases, the distinction is important since it changes the differential diagnosis: new enhancement in a lesion that has been treated with chemoradiotherapy might be due to tumor progression as well as pseudoprogression or radiation necrosis in the appropriate timeframe, whereas the same change in a tumor that has not been treated would be very alarming for tumor progression.

Follow-up imaging should be performed using the same imaging modality as the baseline, which would be MRI in almost all cases [20]. Ideally, the same MRI scanner should be used, but if that is not possible or feasible, at least scanners with same magnet strength should be used (Fig. 2.2) [20].

Some clinical data can help with the interpretation of follow-up images: Type of treatment the patient received and when the treatment was completed would help determine if increasing or new enhancement could be due to pseudoprogression, radiation necrosis, or tumor progression; antiangiogenic therapy might cause decreased enhancement without true regression; changes in steroid dose can affect the size of T2/FLAIR hyperintense component and enhancement; knowledge of the radiation field could help differentiate progression or new disease outside the field from radiation-induced changes [17].

Edema, treatment-related changes, and postoperative gliosis surrounding the surgical cavity might make it difficult to determine the recurrence of the lesion using T2W or FLAIR images. Outside of the timeframe for treatment-related changes, increases in T2/FLAIR hyperintensity should be suspicious for progression of non-enhancing tumor or increasing edema. Similarly new or increasing contrast enhancement, especially outside the high-dose radiation zone, is also a red flag [17].

2.2.5.1 Pseudoprogression

Pseudoprogression is a temporary, new, or increased area of contrast enhancement without true tumor progression, caused by treatment-induced changes [21–23]. It has been described in 10–30% of GBM patients who receive radiotherapy and temozolomide, in GBM patients receiving immunotherapy, and in LGG patients receiving radiotherapy [21, 22, 24]. It occurs most commonly within 3–6 months following therapy [17, 25]. Pseudoprogression may be more frequent in patients with MGMT promoter

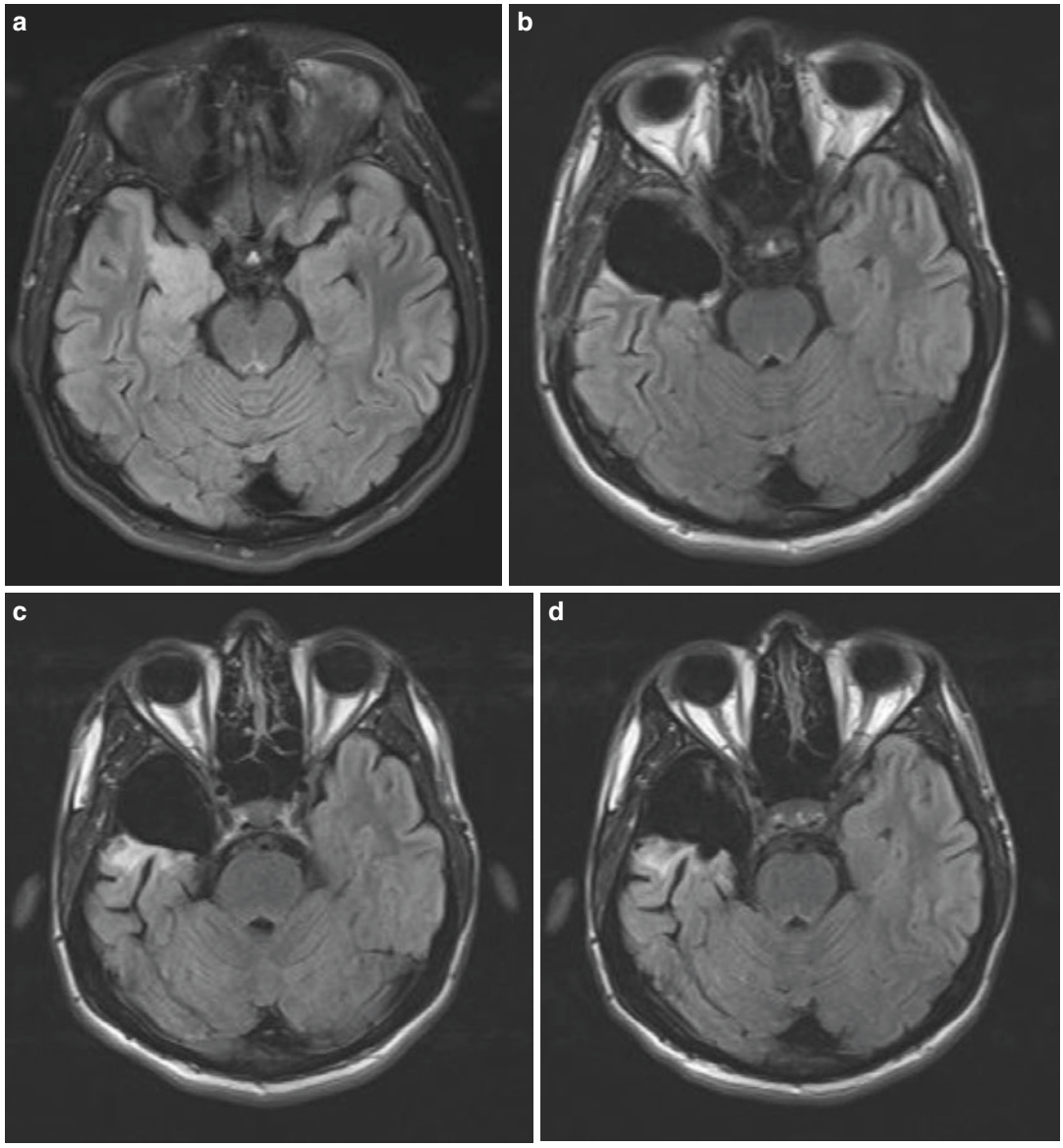

Fig. 2.2 Preoperative and follow-up FLAIR images of a 21-year-old (at time of four year follow-up) male patient with grade II glioma. (**a**) Preoperative, (**b**) 3 months post-op, (**c**) one year post-op, (**d**) four years post-op. Note the changes in FLAIR intensities surrounding the operation cavity, corresponding to gliosis

hypermethylation [17, 22]. Although most patients are asymptomatic, there may be deterioration in neurologic status or an increased need for steroids [22]. It typically resolves spontaneously [21].

Differentiating pseudoprogression from true tumor progression is challenging [24, 26]. Multifocality, the signal abnormality extending across the corpus callosum and subependymal involvement are suggestive of true progression, but there are no definitive conventional MRI findings to rule out true progression reliably [24]. Higher ADC values and lower perfusion parameters have been observed in pseudoprogression compared to true tumor progression [23, 24]; however, the thresholds reported in the literature

should be applied with care [23]. Clinical data can also help with the differential diagnosis: pseudoprogression occurs up to 6 months after treatment, and changes are expected to stabilize or improve in follow-up without any treatment [17, 24].

2.2.5.2 Radiation Necrosis

Another difficulty is radiation necrosis in patients who underwent radiotherapy. Radiation necrosis most commonly occurs 9–12 months after treatment but can be seen years after radiotherapy [17, 22]. Differentiating radiation necrosis from tumor progression is difficult using conventional MRI [17, 27]. Perfusion MRI might be helpful, but there is significant disparity in published results [17].

2.2.5.3 Pseudoresponse

Pseudoresponse or pseudoregression is a decrease in enhancement without a true antitumor effect [17, 22]. It is seen in 20–60% of patients receiving antiangiogenic therapy such as bevacizumab or cediranib and thought to be due to a normalization of abnormally permeable blood vessels which can cause marked decrease in contrast enhancement and peritumoral edema as early as day 1 after treatment [21, 24]. To distinguish this from true antitumor effect, patients under antiangiogenic therapy who demonstrate marked reduction in enhancement need to have another scan at least 4 weeks later to confirm the persistence of changes [18, 28]. Antiangiogenic therapies may select for hypoxic and invasive tumor that first grows as a non-enhancing mass before progressing to enhancing disease [24]. Therefore, careful consideration of T2/FLAIR intense non-enhancing parts of the mass is essential in this subset of patients.

2.3 Evaluating Treatment Response

In patients who underwent treatment, there is an obvious need to report whether the disease is stable, progressing, or regressing in follow-up studies. One way of doing this is simply reporting measurements and/or a subjective assessment by the radiologist. An alternative is creating an objective set of criteria to determine the response to treatment as well as provide a common terminology to be used in radiology reports. This would be beneficial especially for research purposes; however, easy-to-use, consistent, and objective terminology would certainly be useful in daily clinical practice as well. While RECIST criteria are widely used to this end for solid tumors in the body, different sets of rules are used for brain tumors [29].

The first set of such criteria was published by Levin et al. in 1977, followed by WHO oncology response criteria published in 1981 [30, 31]. The more widely used and well-known criteria (commonly referred to as Macdonald criteria) based on CT images, but later extrapolated to MRI, was proposed by Macdonald et al. in 1990. In the paper, the state of the tumor was described as complete response (CR), partial response (PR), stable disease (SD), or progression (progressive disease, PD) (Table 2.1) [32].

However, some limitations of the Macdonald criteria became apparent over time, such as not accounting for pseudoprogression, not evaluating non-enhancing component of the tumor, failing to address pseudoresponse in patients using antiangiogenic treatment, difficulty of measuring irregularly shaped tumors as well as in measuring enhancing lesions located on the walls of cysts or surgical cavities [18, 33]. To address these issues, Response Assessment in Neuro-Oncology (RANO) criteria for high-grade gliomas (RANO-HGG) was proposed in 2010 [18]. These criteria, commonly referred to as the RANO criteria, consider radiologic appearance, corticosteroid use and dose, and clinical status to define CR, PR, SD, or PD (Table 2.1). However, in the following section, only the radiographic criteria will be discussed. Interested readers are referred to the original paper for more information regarding clinical details [18].

Table 2.1 Comparison of various response assessment criteria

	RANO-HGG	RANO-LGG	RANO-BM	iRANO[g]	Macdonald
CR[a,b,d]	– No enhancement[g] – T2/FLAIR Stable to decreased[h] – No new lesions	– No lesion on T2/FLAIR, with complete resolution of enhancement if present before – No new T2/FLAIR abnormalities besides radiation effect – No new/increased enhancement – No new lesion	– No target lesions[j] – No non-target lesions[k] – No new lesions	Same as RANO-HGG, RANO-LGG or RANO-BM based on the type of tumor except for early progression[m]	– No enhancing disease – No new lesion
PR[a,c,d]	– ≥50% decrease in enhancing lesion[g,i] T2/FLAIR Stable to decreased[h] – No new lesions	– ≥50% decrease on T2/FLAIR[i] – No new T2/FLAIR abnormalities besides radiation effect – No new/increased enhancement – No new lesion	– ≥30% decrease in target lesions[j,l] – Stable or improved non-target lesions[k] – No new lesions	Same as RANO-HGG, RANO-LGG or RANO-BM based on the type of tumor except for early progression[m]	– ≥50% decrease in enhancing lesion[i] – No new lesions
SD[a,c,d]	– Enhancing lesion <50% decrease or <25% increase[i] – T2/FLAIR Stable to decreased[h] – No new lesions	– Stable on T2/FLAIR (not qualifying for other categories)[i] – No new T2/FLAIR abnormalities besides radiation effect – No new/increased enhancement – No new lesion	– Between <30% decrease and <20% increase in target lesions[j,l] – Stable or improved non-target lesions[k] – No new lesions	Same as RANO-HGG, RANO-LGG or RANO-BM based on the type of tumor except for early progression[m]	– Enhancing lesion <50% decrease or <25% increase[i] – No new lesions
PD[e,f]	– Enhancing lesion ≥25% increase[i] – Increased T2/FLAIR[h] – New lesion	– ≥25% increase on T2/FLAIR[i] – Increase in enhancement – New lesion	– ≥20% increase in target lesions[j,l] – Unequivocal progression of non-target lesions[k] – New lesion	Same as RANO-HGG, RANO-LGG or RANO-BM based on the type of tumor except for early progression[m]	– Enhancing lesion ≥25% increase[i] – New lesion
Minor Response	N/A	– 25–50% decrease on T2/FLAIR[i] – No new T2/FLAIR abnormalities besides radiation effect – No new/increased enhancement – No new lesion	N/A	If the tumor is LGG, same as RANO-LGG except for early progression[m]	N/A

BM brain metastases, *CR* complete response, *HGG* high-grade glioma, *iRANO* immunotherapy response assessment in neuro-oncology, *LGG* low-grade glioma, *PD* progressive disease, *PR* partial response, *RANO* response assessment in neuro-oncology, *SD* stable disease. Adapted from the relevant references for RANO-HGG, RANO-LGG, iRANO, RANO-BM, and Macdonald criteria [18, 19, 32, 34, 35]

[a]Patient should have all findings to qualify for the category

[b]CR requires the patient to be off corticosteroids or on physiologic replacement dose only

[c]PR and SD require the patient to be at the same or decreased corticosteroid dose compared to baseline scan

[d]CR, PR, and SD require the patient to be stable or improved clinically

Table 2.1 (continued)

[e]Any one of the findings is sufficient to qualify for progression. Neurologic deterioration not attributable to another cause also qualifies for PD by itself. Increase in corticosteroid dose by itself does not constitute PD

[f]To differentiate pseudoprogression from true tumor progression, unless progression is clearly outside the radiation field or there is pathologic confirmation, patients cannot be categorized as having PD within the first 12 weeks after chemoradiotherapy

[g]Findings should persist on a follow-up scan at least 4 weeks later

[h]Significant increase as determined qualitatively

[i]Lesion size measured as longest perpendicular two dimensions on an axial slice and multiplied. If there is more than one lesion, up to five lesions are chosen as described in the RANO-HGG section of the text and products of all lesions are summed to get a single value for comparison

[j]A measurable lesion is a contrast-enhancing lesion that can be accurately measured in at least one dimension, with a minimum size of 10 mm (or twice the slice thickness). The diameter perpendicular to the longest dimension should at least be 5 mm. Up to five largest measurable lesions that can be measured reproducibly can be picked as target lesions. Lesions not treated with local therapies are preferred if present

[k]All measurable lesions besides target lesions and all non-measurable lesions are non-target lesions. They should be recorded at baseline and classified as present, absent or unequivocal progression in follow-up

[l]Only the largest diameter in an axial slice is measured. In cases of multiple target lesions, the diameters are summed to get a single value for comparison in follow-up

[m]If there is radiological progression of lesions within 6 months of starting immunotherapy (including presence of new lesions), follow-up imaging is required 3 months later. If 3-month follow-up scan meet the criteria for CR, PR, or SD then the patient is categorized thus. If the 3-month follow-up scan demonstrates PD, the patient is considered to have PD. If there are new or increasing neurological symptoms not attributable to comorbid events in this time period, the patient is deemed to have PD. If radiological progression occurs more than 6 months after starting immunotherapy, the patient is considered to have PD and 3-month follow-up scan is not required for categorization

2.3.1 Response Assessment in Neuro-Oncology: High-Grade Glioma (RANO-HGG)[1]

RANO-HGG criteria (commonly referred to as only the "RANO criteria") define measurable disease as bidimensionally contrast-enhancing lesion(s) with clearly defined margins on CT or MRI, with two largest perpendicular diameters on an axial slice being at least 10 mm (Fig. 2.3). The lesion should be visible on at least two consecutive axial slices, and the slice thickness must preferably be at most 5 mm with 0 mm gap. If the slice thickness is greater than 5 mm, the size of the lesion should be at least two times the slice thickness to be considered measurable. If the lesion is unidimensionally measurable, lacks clearly defined margins, or smaller than 10 mm (or twice the slice thickness) in at least one dimension, it should be considered nonmeasurable. Special note is made of tumors around a cyst or surgical cavity: such lesions are to be considered nonmeasurable unless they have a clear nodular component that satisfies criteria for being measurable (i.e., at least 10 mm in two perpendicular dimensions).

If there is more than one lesion, two to five of the largest lesions should be measured in two dimensions, the area should be calculated as the product of the two diameters and then the areas of the measured lesions should be added to get a single final value. Comparisons in follow-up should be made using this single value. While typically the largest lesions are selected for measurement, care should be taken to ensure that these lesions allow reproducible measurements. In cases where the largest lesions do not lend themselves to reproducible measurements, the next largest lesion that can be measured reproducibly can be selected instead. The lesions picked for measurement and calculation of the final value for comparison are defined to be the "target lesions."

Non-enhancing components of the tumor are evaluated using T2W or FLAIR images, where they have similar appearance to peritumoral edema and radiation-related changes, making exact delineation of its margins quite difficult.

[1]Adapted from [18].

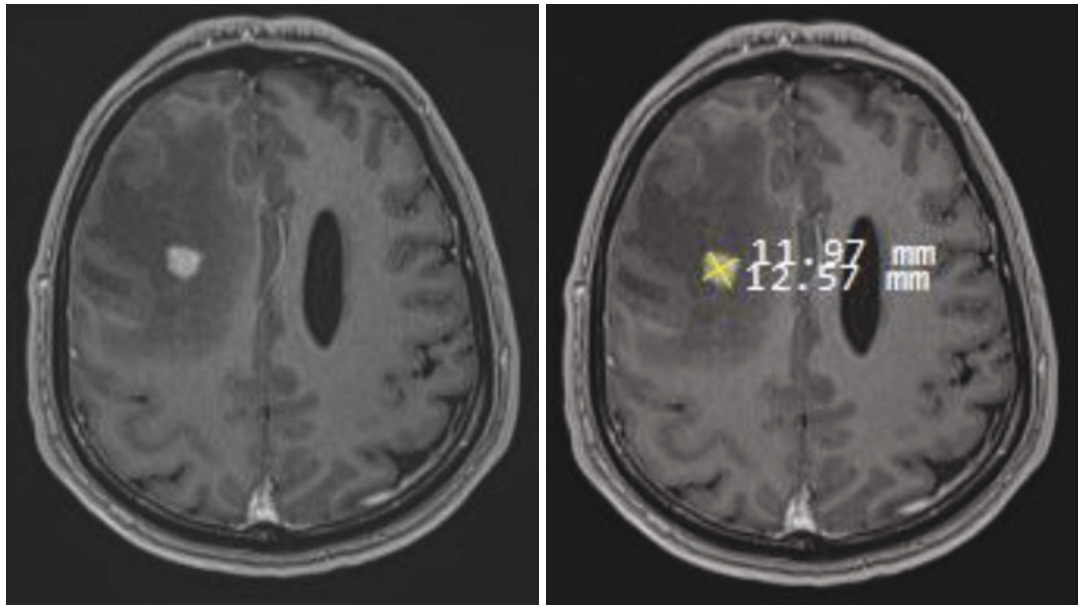

Fig. 2.3 Sample measurement of a high-grade glioma according to RANO criteria. With both dimensions of the enhancing part greater than 10 mm, this constitutes measureable disease

Signs of mass effect such as sulcal effacement or compression of the ventricles; infiltration of the cortical ribbon or simply the location being outside of the radiation field suggest infiltrating tumor. Sometimes, there might still be doubt as to whether the changes represent an increase in non-enhancing tumor. In such cases further follow-up usually confirms or refutes the idea. While objective measures of non-enhancing tumor would obviously be helpful, there are no widely accepted methods for this purpose and RANO criteria do not incorporate any such methods yet.

Response is determined in comparison to the baseline imaging to determine CR or PR, and the smallest tumor measurement (in pre-treatment baseline images or in follow-up images after the initiation of treatment) to determine PD. In cases where the changes are equivocal, close follow-up is indicated. Rules to classify response are provided in Table 2.1.

2.3.2 Other RANO Criteria

Patients receiving immunotherapy and patients with other types of brain tumors should not be evaluated using RANO-HGG criteria. There are different criteria described for brain metastases (RANO-BM), low-grade gliomas (RANO-LGG), and patients undergoing immunotherapy (iRANO) [19, 34, 35]. Major differences of these criteria and how they compare to RANO-HGG are provided in Table 2.1. Response assessment for leptomeningeal metastases (RANO-LM) is handled in a totally different manner and interested readers are referred to the original paper for details on how to score imaging data [36]. Criteria for spine tumors (SPINO), pediatric brain tumors (RAPNO), and meningiomas (RANO-meningioma) are also under development [37–39].

2.4 Imaging Protocol

To standardize neuro-oncologic imaging in clinical trials, Consensus Recommendations for a Standardized Brain Tumor Imaging Protocol (BTIP) have been reported [20]. While this protocol is concerned mostly with standardizing MRI acquisition to facilitate multicenter studies and comparison of different studies, it is also recommended to be used for routine, clinical brain tumor imaging [33]. According to BTIP, MRI

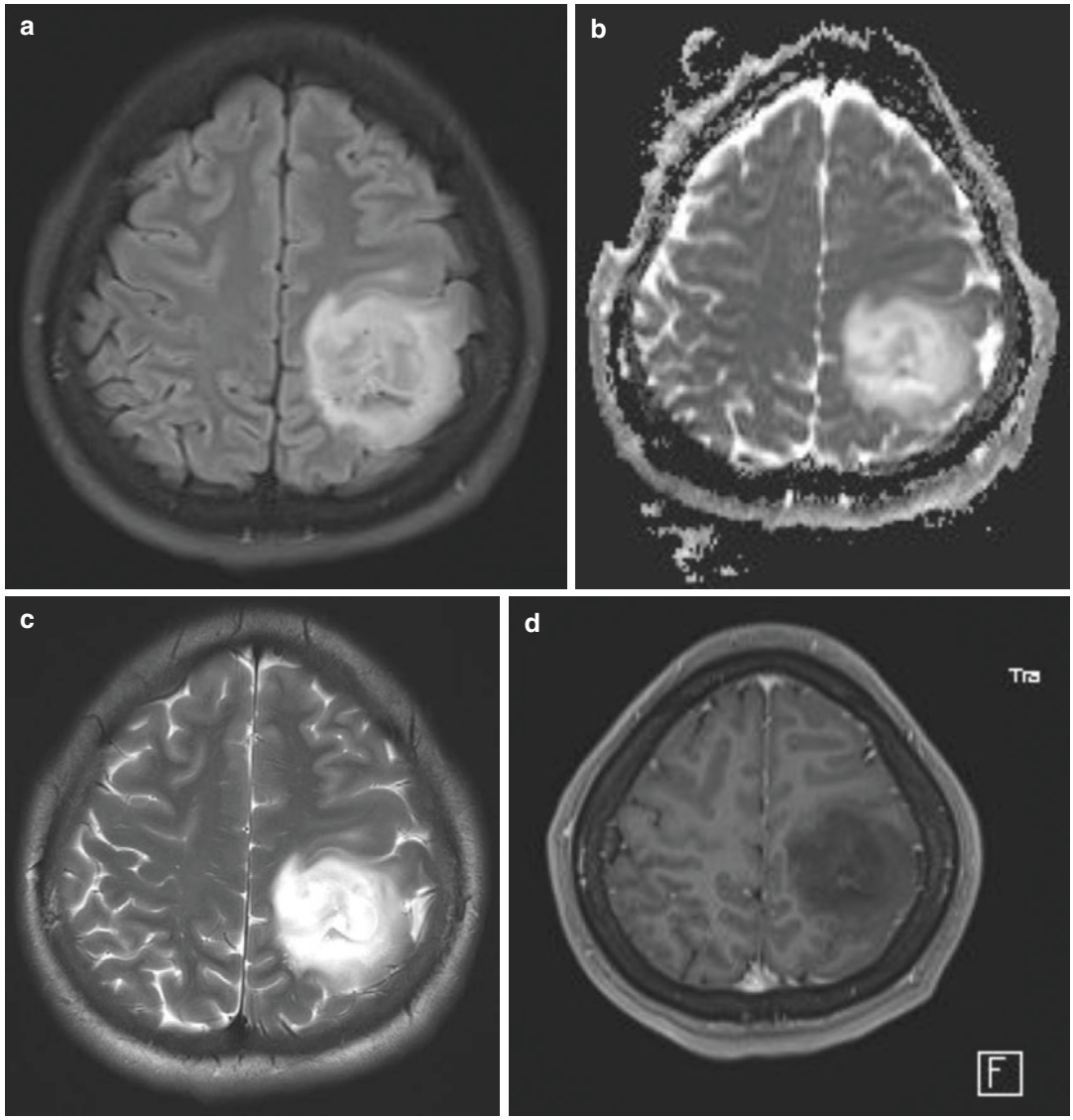

Fig. 2.4 Sample images for brain tumor imaging according to the recommended protocol: (**a**) 2D FLAIR, (**b**) ADC map acquired from DWI using 3 directions and b values 0, 500 and 1000 s/mm^2, (**c**) 2D T2W, (**d**) post-contrast 3D T1W. It should be noted that T1W images were acquired in the sagittal plane but are here demonstrated in the axial plane (using MPR) to be consistent with other images

imaging of brain tumors should include at least the following sequences (Fig. 2.4) [20]:

- Pre-contrast and post-contrast isotropic 3D inversion recovery-prepared T1W gradient-recalled echo (IR-GRE) images with matching parameters
- Axial 2D T2W TSE (dual echo preferred but not required) acquired after contrast injection but before post-contrast T1W images
- Pre-contrast axial 2D TSE T2W FLAIR
- Pre-contrast axial 2D three-directional DWI using echoplanar (EPI) or radial acquisition

The scanner used may be 1.5 T or 3 T [20]. There have been studies reported on 7 T scanners, but whether the use of 7 T scanners would translate into clinical benefit within the context of brain tumors is not clear [40]

Specific acquisition parameters as described by the consensus statements are provided in Table 2.2 [20]

Table 2.2 Consensus recommendations for a standardized brain tumor imaging protocol; recommended protocols for 3 T and 1.5 T scanners

	Pre-contrast T1W[a]		FLAIR[e]		DWI[h]		IV Contrast injection[j]	T2W[k]		Post-contrast T1W[a,l]	
Sequence	IR-GRE[b]		TSE[f]		EPI[i]			TSE[f]		IR-GRE[b]	
Plane of acquisition	Sagittal/axial[c]		Axial		Axial			Axial		Sagittal/axial[c]	
3D/2D	3D		2D		2D			2D		3D	
Field strength	3 T	1.5 T	3 T	1.5 T	3 T	1.5 T		3 T	1.5 T	3 T	1.5 T
TR (ms)	2100[d]	2100[d]	>6000	>6000	>5000	>5000		>2500	>3500	2100[d]	2100[d]
TE (ms)	Min	Min	100–140	100–140	Min	Min		80–120	100–120	Min	Min
TI (ms)	1100[d]	1100[d]	2500	2200	–	–		–	–	1100[d]	1100[d]
Flip angle	10–15°	10–15°	90°/≥160°	90°/≥160°	90°/180°	90°/180°		90°/≥160°	90° ≥ 160°	10–15°	10–15°
Frequency	256	≥172	≥256	≥256	128	128		≥256	≥256	256	≥172
Phase	256	≥172	≥256	≥256	128	128		≥256	≥256	256	≥172
NEX	≥1	≥1	≥1	≥1[g]	≥1	≥1[g]		≥1	≥1[g]	≥1	≥1
FOV (mm)	256	256	240	240	240	240		240	240	256	256
Slice thickness (mm)	1	≤1.5	3	≤4[g]	3	≤4[g]		3	≤4[g]	1	≤1.5
Gap/spacing	0	0	0	0	0	0		0	0	0	0
Parallel imaging	Up to 2×	No	Up to 2×	Up to 2×	Up to 2×	Up to 2×		Up to 2×	Up to 2×	Up to 2×	No

Adapted from [20]

DWI diffusion-weighted imaging, *EPI* echo planar imaging, *FLAIR* fluid attenuated inversion recovery, *FOV* field of view, *FSE* fast spin echo, *GRAPPA* generalized autocalibrating partial parallel acquisition, *IR-GRE* inversion recovery gradient-recalled echo, *NEX* number of excitations, *PD* proton density, *SNR* signal-to-noise ratio, *TE* echo time, *TI* inversion time, *TR* repetition time, *TSE* turbo spin echo

[a]Post-contrast T1W images should have identical parameters to pre-contrast T1W images

[b]3D acquisitions without inversion preparation should be avoided

[c]Sagittal preferred due to fewer required slices and thus shorter scan times

[d]The values provided are for Siemens and Hitachi scanners. GE, Philips and Toshiba scanners should use *TR* = 5–15 ms and *TI* = 400–450 ms

[e]3D FLAIR images are strongly endorsed, due to the possibility of multiplanar reconstruction, volumetry and less sensitivity to flow artifacts; but are considered optional due to not being universally available. The following parameters are recommended for 3D FLAIR: *TE* = 90–140 ms, *TR* = 6000–10,000 ms, *TI* = 2000–2500 ms (chosen based on vendor recommendations), GRAPPA ≤2, fat saturation, slice thickness ≤1.5 mm, FOV ≤250 mm × 250 mm, matrix ≥244 × 244, sagittal or axial acquisition

[f]TSE is equivalent to FSE in GE, Hitachi, and Toshiba scanners

[g]To get comparable SNR, older 1.5 T scanners can use images with 5 mm slice thickness with no interslice gap or increase NEX for slice thickness ≤4 mm

[h]DWI images should be acquired in at least 3 directions with $b = 0$, 500 and 1000 s/mm^2. If the scanner is an older scanner incapable of at least three b values, $b = 0$, 1000 s/mm^2 should be used

[i]If there is significant patient motion, radial acquisition schemes may be used. However, this should be a last option

[j]0.1 mmol/kg (up to 20 cc) gadolinium-chelated contrast injection at a rate of 3–5 cc/s, preferably using a power injector, as a single, full dose

[k]Dual echo PD/T2 TSE is optional. If used, the PD echo should have a TE <25 ms

[l]Advanced sequences can be substituted before the post-contrast T1W images as long as post-contrast 3D T1W sequences are acquired between 4–8 min following contrast administration

Other sequences such as high-resolution isovolumetric 3D T2W images and advanced imaging techniques can be included in the study based on clinical indications and whether they are needed for differential diagnosis or surgical planning, but are not included in the minimum required study. The protocol also allows for other additional post-contrast T1W imaging, such as 2D fat-saturated T1W TSE images. However, such images should be acquired after the recommended 3D T1W images to ensure consistency of the timing of the contrast injection and 3D T1W image acquisition.

Perfusion-weighted imaging has not yet made its way into standardized imaging protocols or treatment response criteria. Nonetheless, perfusion studies are very helpful during follow-up, to differentiate recurrence from treatment-related changes such as radiation necrosis or pseudo-progression. In the proper clinical setting, these images are invaluable as problem solvers and in our opinion should be included in every follow-up study where it is technically possible to do so. With dynamic susceptibility contrast (DSC) studies, tumor recurrence is expected to have a higher relative cerebral blood volume (rCBV) than radiation necrosis or pseudoprogression; however, there is considerable overlap and the findings can be dependent on the technique used [17]. Therefore, clinical findings and, more importantly, correlation with conventional MRI images are essential for an accurate diagnosis. A more detailed explanation of perfusion imaging is provided in another chapter of this book.

2.4.1 Contrast Use

0.1 mmol/kg gadolinium-chelated contrast agent should be injected at an injection rate of 3–5 cc/s with a power injector if possible [20]. The same contrast agent must be used for follow-up; in cases where this is not possible, at least contrast agents with the same chemical composition should be used [20]. Images should be acquired 4–8 min after contrast injection [20].

Regarding adverse reactions, complications and contraindications of gadolinium-based contrast agents, and their use in special patient groups such as children, those with renal failure, or pregnant women, relevant national or international guidelines such as ACR Manual on Contrast Media (https://www.acr.org/Clinical-Resources/Contrast-Manual) [41] or ESUR Guidelines on Contrast Agents (http://www.esur-cm.org/index.php/en/) [42] should be followed.

2.5 Conclusion

MRI is the preferred imaging method to diagnose and follow-up brain tumors. Consensus statements regarding imaging protocols recommend, at a minimum, 3D isotropic T1W parameter matched pre- and post-contrast images, 2D T2W and 2D FLAIR images, DWI using 3 b values (b = 0, 500, and 1000 s/mm^2) in at least three directions. Other advanced imaging methods are also useful and may be included in the routine protocol or on a case-by-case basis as needed.

MRI is essential for surgical planning, where advanced imaging modalities such as DTI and fMRI can be very useful. Intraoperative MRI can improve tumor resection, and thus prognosis. Postoperative imaging is necessary to ensure tumor resection and to provide baseline images for follow-up.

Follow-up is mainly concerned with the size of enhancing lesion as well as non-enhancing mass as demonstrated by T2W/FLAIR images. Based on the treatments used and the timeframe, pseudoresponse, pseudoprogression, and radiation necrosis should be taken into consideration where appropriate. DWI and perfusion images are very useful as problem solvers and to increase confidence in diagnosis of recurrence or treatment-related changes. Depending on whether the tumor is primary or metastatic, its histopathological type and grade, and the use of immunotherapy, different criteria to evaluate treatment response have been proposed and their use provide objective methods to assess response as well as a common terminology to use in reporting.

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