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REVIEW ARTICLE

Imaging of oligodendroglioma

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ABSTRACT

Oligodendroglioma are glial tumours, predominantly occurring in adults. Their hallmark molecular feature is codeletion of the 1p and 19q chromosome arms, which is not only of diagnostic but also of prognostic and predictive relevance. On imaging, these tumours characteristically show calcification, and they have a cortical–subcortical location, most commonly in the frontal lobe. Owing to their superficial location, there may be focal thinning or remodelling of the overlying skull. In contrast to other low-grade gliomas, minimal to moderate enhancement is commonly seen and perfusion may be moderately increased. This complicates differentiation from high-grade, anaplastic oligodendroglioma, in which enhancement and increased perfusion are also common. New enhancement in a previously non-enhancing, untreated tumour, however, is suggestive of malignant transformation, as is high growth rate. MR spectroscopy may further aid in the differentiation between low- and high-grade oligodendroglioma. A relatively common feature of recurrent disease is leptomeningeal dissemination, but extraneural spread is rare. Tumours with the 1p/19q codeletion more commonly show heterogeneous signal intensity, particularly on T_2 weighted imaging; calcifications; an indistinct margin; and mildly increased perfusion and metabolism than 1p/19q intact tumours. For the initial diagnosis of oligodendroglioma, MRI and CT are complementary; MRI is superior to CT in assessing tumour extent and cortical involvement, whereas CT is most sensitive to calcification. Advanced and functional imaging techniques may aid in grading and assessing the molecular genotype as well as in differentiating between tumour recurrence and radiation necrosis, but so far no unequivocal method or combination of methods is available.

INTRODUCTION

Oligodendroglioma are glial tumours, together with mixed oligoastrocytoma constituting 5–20% of all gliomas.[1] They occur predominantly in adults, with a peak between 40 and 60 years of age and patients with low-grade tumours being slightly younger than those with high-grade, anaplastic tumours. Although oligodendroglioma are sometimes considered relatively benign because of their initial indolent disease course, they are almost invariably fatal. Most oligodendroglioma occur in the cerebral white matter, but they can be found anywhere in the central nervous system.

The molecular hallmark feature of oligodendroglioma is codeletion of the short arm of chromosome 1 (1p) and the long arm of chromosome 19 (19q),[2] which is present in about 60–90% of histopathologically diagnosed oligodendroglioma.[1] Mixed oligoastrocytoma also commonly harbours the 1p/19q co-deletion, although less frequently (30–50%) than oligodendroglioma.[3] As the name implies, the diagnosis of oligoastrocytoma requires the presence of both a neoplastic oligodendroglial and neoplastic astrocytic component. There is, however, no uniform threshold for the proportion of the astrocytic component, resulting in considerable variation in the histopathological diagnosis of oligoastrocytoma.[4]

In their recently published consensus guidelines for nervous system tumour classification and grading, coined the "Haarlem Consensus", the International Society of Neuropathology proposes that both histopathologically diagnosed oligodendroglioma and oligoastrocytoma with the 1p/19q co-deletion are classified as oligodendroglioma.[5] Tumours without the 1p/19q codeletion would be classified as "diffuse glioma of the oligodendroglial phenotype" in cases of histopathological appearance of oligodendroglioma and as "diffuse astrocytoma" in cases of histopathological appearance of oligoastrocytoma. According to these guidelines that incorporate molecular information into brain tumour classification, the diagnosis of oligoastrocytoma would thus cease to exist.

In addition to having diagnostic value, the 1p/19q codeletion also has prognostic and predictive relevance as was shown in two major randomized controlled trials.[6,7] Early procarbazine, lomustine and vincristine added to radiotherapy greatly increases survival in patients with anaplastic

oligodendroglioma, compared with radiotherapy alone. This treatment regime is now the standard of care for patients with 1p/19q codeleted anaplastic oligodendroglioma.

The role of imaging in patients with oligodendroglioma falls into three main categories: (1) diagnostic work-up; (2) surgical and radiotherapy guidance; and (3) follow-up and treatment monitoring. Structural MRI is the workhorse imaging technique for all of these indications, while there is a small, complementary role for CT. Advanced MRI and functional imaging techniques are also increasingly used in the clinical routine. These include diffusion-weighted imaging (DWI), perfusion imaging, MR spectroscopy and positron emission tomography (PET) imaging. Main indications for these techniques are tumour grading and the distinction between tumour progression and treatment effects, most notably radiation necrosis.

In this article, the imaging features of oligodendroglioma are reviewed, distinguishing between the routinely used structural imaging techniques in the first section, and advanced and functional imaging techniques in the second section. In both sections, the differential diagnostic considerations, features of high-grade disease or transformation and the differentiation between tumour progression and treatment effects are addressed. In the third section, the imaging features of the 1p/19q codeletion are described, both using structural and functional imaging techniques.

STRUCTURAL IMAGING

For brain tumour imaging in general, MRI is the modality of choice, delivering a wide range of imaging contrasts, which allows for much better intrinsic tissue discrimination than CT.

Imaging characteristics

The hallmark features of oligodendroglioma are the presence of calcification and a cortical-subcortical location. Neither on CT nor on MRI can pure oligodendroglioma reliably be distinguished from mixed oligoastrocytoma, although some imaging features appear to be more commonly present in one or the other tumour type, as specified below.[8] In the paediatric population, calcification, peritumoural oedema and contrast enhancement are less commonly seen than in adults.[3]

On non-enhanced CT, coarse calcification is reported in up to 90% of cases (Figure 1). A gyriform band of cortical mineralization makes the diagnosis of oligodendroglioma particularly likely.[9] In fact, oligodendroglioma is the most common brain tumour to calcify.[3] In small oligodendroglioma, however, calcification may not be seen. On MRI, calcification may be less prominent or not at all visible (Figure 1) and have variable signal intensity adding to the heterogeneous appearance of the tumour. It has been suggested that calcification is less common in mixed oligoastrocytoma than in pure oligodendroglioma.[3]

Oligodendroglioma are typically hypodense on CT, but heterogeneity of density (mixed hypo-/isodense) is also commonly seen. Rarely, the tumour is hyperdense. Small oligodendroglioma may not be visible on CT, and MRI is superior to CT in delineating the tumour.[3] Signal intensity on MRI is generally lower than that of the grey matter on T_1 weighted sequences. On T_2 weighted imaging, the tumour is hyperintense with commonly marked heterogeneity (Figure 2).[10] Cystic degeneration and haemorrhage may occur, but these are not frequent findings. Peritumoural oedema is also not common. Such features tend to point towards anaplastic degeneration of the tumour.

After intravenous contrast administration, oligodendroglioma generally do not enhance. Minimal to moderate patchy, multifocal enhancement with a dot-like or lacy pattern is, however, reported in up to 50% of cases (Figure 3).[10,11] This distinguishes oligodendroglioma from other low-grade gliomas that do not enhance and has been suggested to be more common in mixed oligoastrocytoma than in oligodendroglioma.[3] It is thought that the so-called "chicken-wire" network of capillaries, characteristically seen on histopathological examination, underlies the contrast enhancement seen in these low-grade tumours. Care needs to be taken, however, not to falsely diagnose contrast enhancement on MRI, as spontaneous hyperintensity on T_1 weighted may be present in the context of calcification or haemorrhage (Figure 4). The non-enhanced T_1 weighted images therefore need to be carefully scrutinized before contrast

Figure 1. Transverse non-enhanced CT, T_1 weighted (T1w) and T_2 weighted (T2w) MRI sections, showing extensive, gyriform calcifications (arrows) on CT in the left frontal lobe. Note that the calcifications are only barely visible on T_1w images as discrete linear hyperintensities (arrows) and are not at all visible on T_2w imaging.

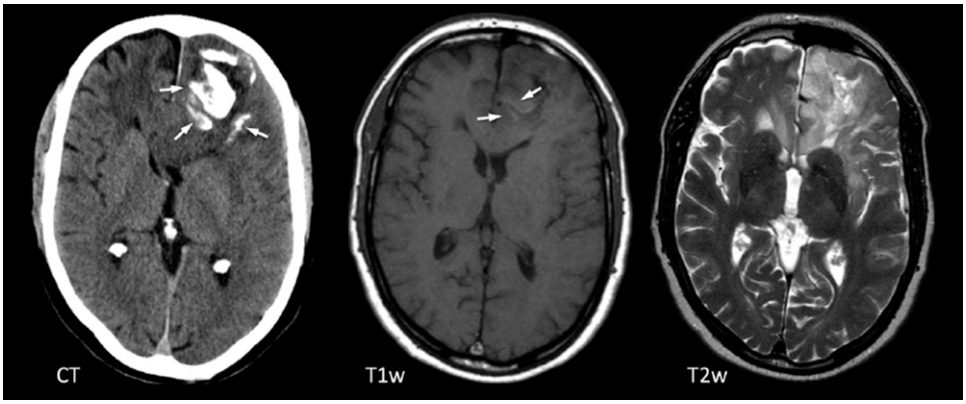
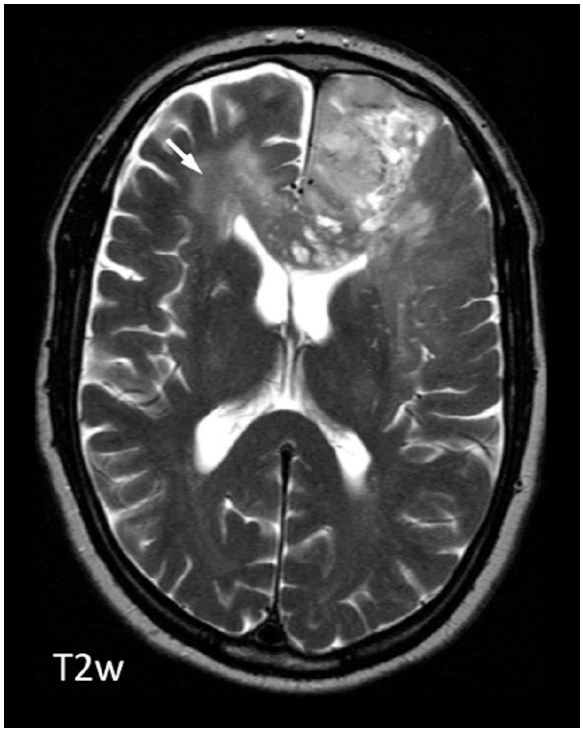


Figure 2. Transverse T_2 weighted (T2w) MRI section showing hyperintensity and marked heterogeneity of signal in a left frontal lobe oligodendroglioma. Note extension of the lesion through the corpus callosum to the right frontal lobe (arrow), creating a "butterfly glioma" appearance.



enhancement can be determined with certainty. Although anaplastic tumours tend to enhance somewhat more frequently, the presence of contrast enhancement is not a reliable imaging feature to grade oligodendroglioma. In one study, the presence of contrast enhancement only had 63% sensitivity and 50% specificity to differentiate high- from low-grade tumours.[11]

Appearance and location

Oligodendroglioma is generally round to oval appearing as a relatively well-circumscribed mass of variable size. In shape, it resembles low-grade diffuse astrocytoma, but oligodendroglioma, in contrast to diffuse astrocytoma, has a characteristic affinity for the cortex.[10] It is typically superficially located, involving both the cortex and the subcortical white matter. Cortical involvement is best appreciated on T_2 fluid-attenuated inversion recovery imaging as (extensive) cortical thickening (Figure 5).[9] Owing to its peripheral location, focal thinning, remodelling or even erosion of the overlying skull is not uncommon (Figure 6).

The majority of tumours are located supratentorially (85%), with the frontal lobe being the most common location (50–65%). A "butterfly glioma" pattern may be seen when a frontal lesion extends through the corpus callosum (Figure 2).[3] Infratentorial location is rare. Extremely rare primary locations are within the ventricular system, brain stem, spinal cord, retina and leptomeninges.[10] It is thought that many of the reported intraventricular oligodendroglioma are in fact misclassified neurocytoma, since they appear to have distinctly different imaging features. In contrast to intraparenchymal oligodendroglioma, intraventricular oligodendroglioma are generally hyperdense on CT and almost always shows enhancement after contrast administration.[3] Primary leptomeningeal involvement is, in contrast to secondary leptomeningeal spread, extremely rare. It is characterized by diffuse enhancement of the leptomeninges, with no parenchymal involvement, and is generally indistinguishable on imaging from (chronic) meningitis.[12] Distinction between intraventricular oligodendroglioma and central neurocytoma, on the other hand, is difficult upon histopathological examination and generally relies on immunohistochemistry or ultrastructural examination.[13]

Differential diagnosis

The most important differential diagnosis of oligodendroglioma is anaplastic oligodendroglioma. As described below, these

Figure 3. Transverse T_1 weighted (T1w) and contrast-enhanced T_1 weighted (cT1w) MRI sections, showing discrete, dot-like enhancement (arrow) in a right frontal lobe oligodendroglioma.

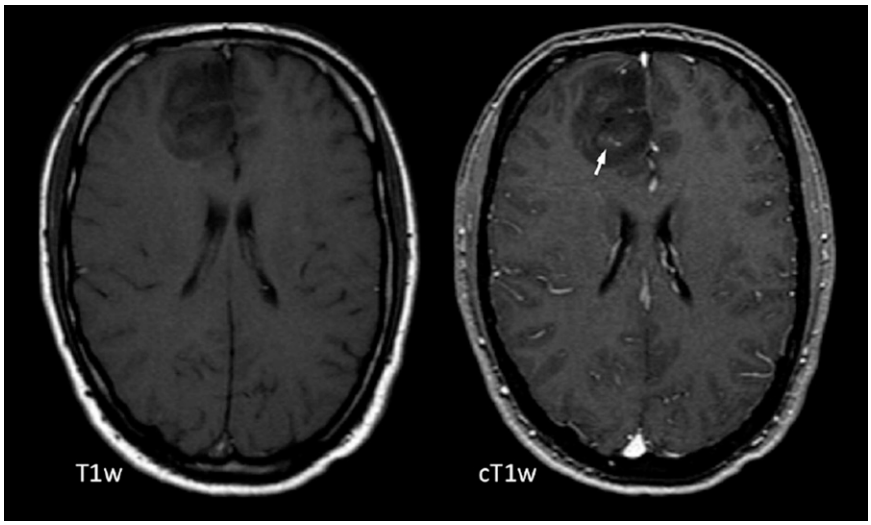
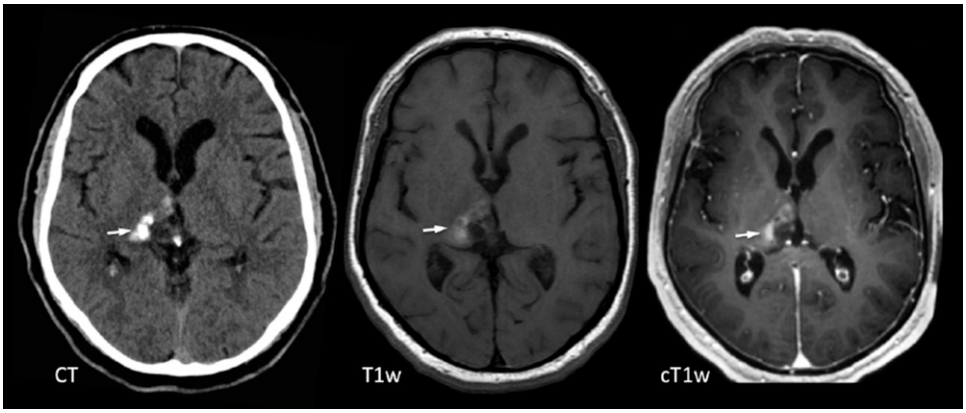


Figure 4. Transverse CT, T_1 weighted (T1w) and contrast enhanced T_1 weighted (cT1w) MRI sections, showing course calcifications (arrows) in the right thalamus, which are hyperintense on the T_1w image and can easily be mistaken for contrast enhancement.



tumours of different World Health Organisation (WHO) grade cannot be reliably distinguished on conventional imaging.

The differential diagnosis on imaging includes other tumours such as low-grade diffuse astrocytoma, ganglioglioma, dysembryoplastic neuroepithelial tumour and pleomorphic xanthoastrocytoma. Although the latter three all have a similar cortical localization to oligodendroglioma, and calcification also being a prominent feature of ganglioglioma, these are all tumours typically occurring in a younger patient population. Although low-grade diffuse astrocytoma less commonly shows calcification and generally spares the cortex, it may be indistinguishable on conventional imaging from oligodendroglioma. When the tumour has an intraventricular location, central neurocytoma is an important and in fact more likely differential diagnosis than oligodendroglioma, which, as mentioned above, is extremely rare within the ventricular system.

Non-neoplastic cortically located lesions such as cerebritis and cerebral ischaemia need to be considered in the differential diagnosis, but generally do not pose great diagnostic difficulty when taking other features, such as diffusion restriction or vascular territories, into account.[14] An important pitfall is thrombosed arteriovenous malformation. When entirely thrombosed, distinctive flow voids are absent, whereas gyriform calcifications may be prominent, rendering the lesion indistinguishable from oligodendroglioma on imaging.[14]

Anaplastic oligodendroglioma

As with low-grade tumour, anaplastic oligoastrocytoma imaging findings mirror those of anaplastic oligodendroglioma and a distinction cannot be made reliably on CT or MRI. Anaplastic oligodendroglioma often has similar imaging features to oligodendroglioma, with no reliable prediction of tumour grade on conventional imaging. Oedema, haemorrhage, cystic degeneration and contrast enhancement are more commonly seen in anaplastic oligodendroglioma (Figure 7), reflecting histopathological findings, but may also be seen in oligodendroglioma. Sometimes, ring-like contrast enhancement may be seen such as classically associated with glioblastoma.[3]

Figure 5. Transverse (left) and coronal (right) T_2 fluid-attenuated inversion recovery MRI sections, showing hyperintensity and thickening of the cortex in a left frontal lobe oligodendroglioma.

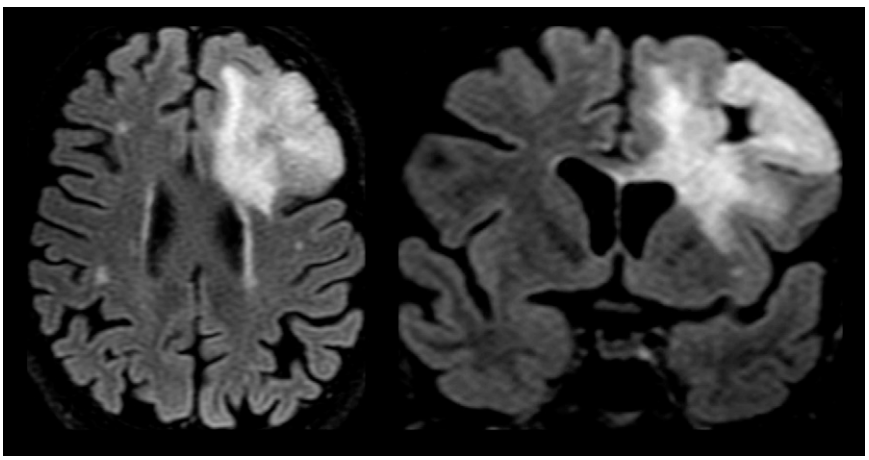
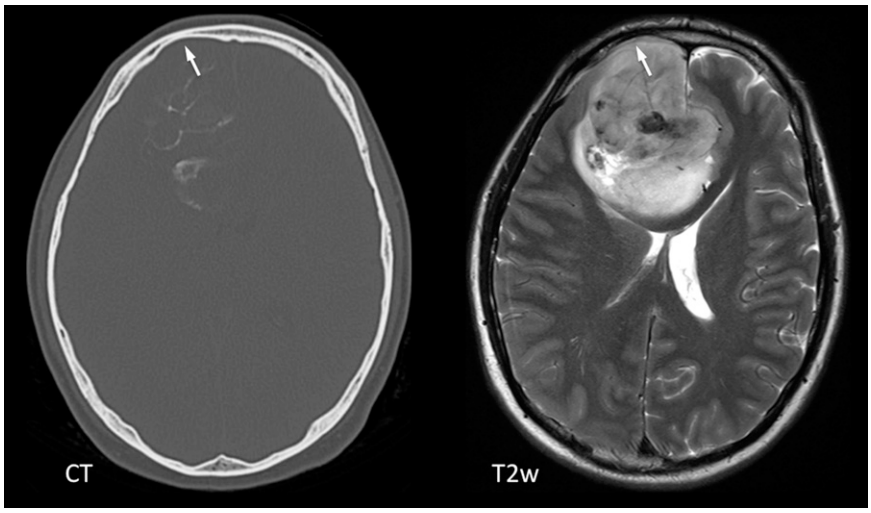


Figure 6. Transverse CT in bone window and T_2 weighted (T2w) MRI sections, showing remodelling of the skull's inner table (arrows) overlying a right frontal lobe oligodendroglioma.



Histopathological examination of tumour tissue therefore remains mandatory. Sampling error, particularly when only biopsy is performed, however, may lead to undergrading of the tumour. Imaging features therefore still need to be taken into account, both for clinically driven tumour grading[1] and to guide biopsy towards (enhancing) tumour regions that are most likely reflecting high-grade tissue.

New enhancement in a previously non-enhancing, untreated tumour is suggestive of malignant transformation.[10] Along similar lines, a high growth rate of the mean tumour diameter (>8 mm per year) is associated with shorter survival time, and tumours with >50% increase in growth over 6 months are more likely to be progressive.[8]

Disseminated and metastatic disease

In contrast to patients with recurrent disease, leptomeningeal dissemination of oligodendroglioma in newly diagnosed patients is rare, obviating the need for routine imaging of the craniospinal axis.[1] Leptomeningeal seeding is not infrequent in recurrent disease, and the cisternal and subarachnoid spaces therefore need to be carefully scrutinized for pathological, nodular enhancement (Figure 8). Larger nodules may also be apparent as hypointense lesions on T_2 weighted images but contrast administration is mandatory for optimal sensitivity.

Extraneural metastases of (anaplastic) oligodendroglioma are rare, although less so than with other tumours of the central nervous system, and are now more frequently seen presumably due to increased survival.[3] These most commonly involve the bone, lymph nodes, lung, pleura and liver and are more frequently seen in patients who received early radiation and chemotherapy.[3]

Treatment effects

Brain tumour follow-up with imaging is hampered by treatment effects with imaging features that may be indistinguishable from (malignant) tumour progression. Such treatment-related effects, most notably radiation-induced injury, hinder the adequate adjustment of therapy. Radiation-induced injury can be divided into acute (1–6 weeks during or after treatment), early delayed (after 3 weeks to several months) and late delayed (after months

Figure 7. Transverse CT, T_2 weighted (T2w) and contrast enhanced T_1 weighted (cT1w) MRI sections, showing a left temporoparietal lobe anaplastic oligodendroglioma with calcification (CT: arrow), cystic degeneration (T2w: arrow), oedema (T2w: arrowheads) and ring-like enhancement (cT1w: arrow).

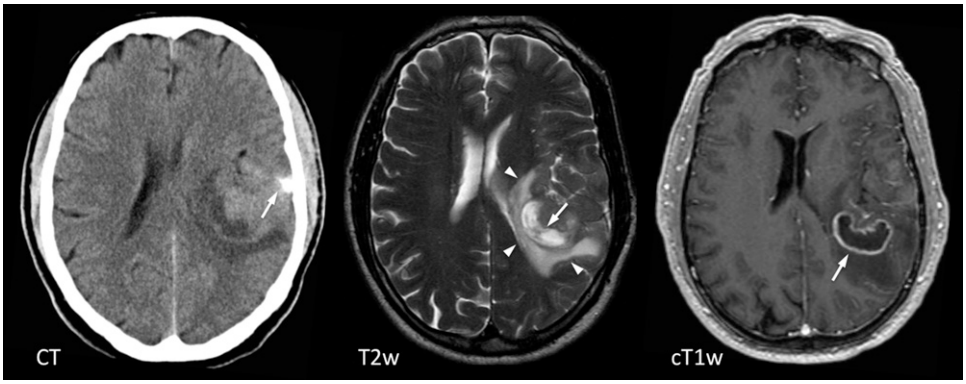
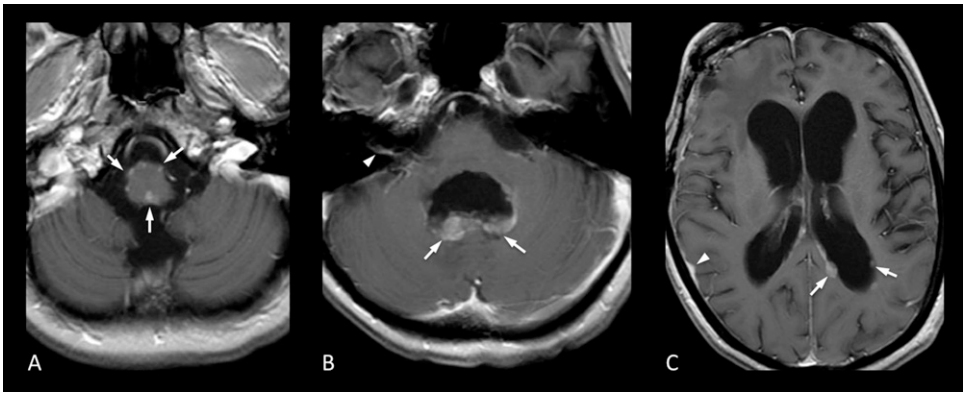


Figure 8. Transverse contrast-enhanced T_1 weighted sections at the level of the medulla oblongata (a), fourth ventricle (b) and lateral ventricles (c), showing leptomeningeal seeding in recurrent anaplastic oligodendroglioma. Note the nodular enhancement surrounding the brain stem (a: arrows); lining the fourth ventricle (b: arrows) and along the cranial nerves in the right internal auditory canal (b: arrowhead); the ventricular wall (c: arrows) and the dura (c: arrowhead).



to years) injury.[10] On conventional MRI radiation necrosis may show increased or new contrast enhancement and/or increased regions of white matter hyperintensity on T_2 weighted images.

Advanced and functional imaging

Conventional CT and MRI techniques fall short in several clinically relevant, diagnostic dilemmas. Most notably, these are the distinction between oligodendroglioma and anaplastic oligodendroglioma, and between treatment effect and tumour recurrence or progression. Advanced and functional imaging techniques aim to visualize and quantify the lesion's microstructure, perfusion, metabolites and metabolism to obtain more sensitive and pathophysiological diagnostic markers of disease. These include DWI, perfusion imaging, MR spectroscopy and PET, respectively.

Diffusion-weighted imaging

DWI measures and quantifies the diffusion of water molecules, or Brownian motion, in tissue.[15] Barriers such as cell membranes, with which the water molecules collide, hinder diffusion. Compared with the normal free diffusion, a lower apparent diffusion coefficient (ADC) is measured in tissue. The ADC increases with tissue damage and with the presence of increased extracellular fluid, such as in vasogenic oedema. Conversely, the ADC is decreased (often called "diffusion restriction") with reduction of the extracellular space. In the context of brain tumour imaging, tortuosity of the interstitial space is presumed to underlie the inverse relationship of ADC with cellular density.[16]

Diffusion restriction is typically absent in oligodendroglioma.[10] Although average ADC values are reported to be lower in high-grade than in low-grade glioma, overlap of values is such that DWI can not reliably distinguish oligodendroglioma from anaplastic oligodendroglioma.[16] This is at least in part due to the fact that in high-grade tumour vasogenic oedema and necrosis, both resulting in high ADC, and vital tumour, with high cellularity and thus lower ADC, coexist. Better results may be obtained when areas of necrosis are excluded from the measurements,[17] but even then such a wide range of ADC values is measured that it is unlikely that a threshold to dichotomize recurrent and stable disease will be established. An alternative approach is to assess ADC measurements longitudinally on a voxel-by-voxel basis.[18] This method is termed functional diffusion mapping and, when combined with traditional tumour diameter measurements, seems to be an accurate predictor of survival in gliomas in general. However, until such advanced post-processing tools become available for the clinical routine, the application of functional diffusion mapping remains primarily in the research arena.

Perfusion imaging

The most commonly used perfusion parameters for brain tumour assessment are cerebral blood volume (CBV) and the volume transfer coefficient (K^{trans}).

CBV is estimated by imaging the first passage of a contrast bolus through the brain parenchyma, either using MR or CT imaging. Since a large number of images of the brain need to be acquired, radiation exposure is an issue, and CT is therefore not routinely performed for this indication. Dynamic susceptibility contrast (DSC) imaging is the term commonly used for this perfusion technique when using MRI.[19] DSC imaging requires about 2 min' of scanning time and makes use of the T_2 and T_2^*-shortening properties of gadolinium-containing contrast media. Typically, the entire brain is imaged in 2 s or less, and approximately 60 whole-brain images are acquired in rapid succession to capture the signal drop with the passage of contrast media through the brain. The measured signal change is considered to be a relative measure of CBV (hence commonly termed *relative* or *r*CBV). Since this measurement is not absolute, rCBV is commonly expressed as a ratio of rCBV in the tissue of interest over rCBV in reference tissue (typically the normal appearing white matter contralateral to the affected hemisphere). It is important to realize that with contrast leakage through the blood–brain barrier, such as is commonly the case in oligodendroglioma, T_1 shortening also occurs. This affects the T_2/T_2^* signal intensity curve and may lead to an inaccurate estimate of rCBV.[20] This effect may be corrected for by post-processing algorithms and most effectively by saturating the tissue with

a preload contrast bolus administered 5–10 min prior to perfusion imaging.[20,21]

rCBV is the most widely used parameter for glioma grading. The angiogenic activity of high-grade tumours results in the presence of increased microvascular density and many slow-flowing collateral vessels, resulting in an increase of rCBV. In their hallmark article, Law et al[22] showed that using a rCBV ratio cut-off value of 1.75, high-grade glioma can be differentiated from low-grade glioma with 95% sensitivity. Unfortunately, these findings do not seem to apply to oligodendroglioma and oligoastrocytoma, which may have markedly elevated rCBV even when low-grade, and in which a reliable distinction between high- and low-grade tumours can not consistently be made.[16,23,24] This finding is considered to be—at least in part—the reason for the relatively low specificity (70%) reported by Law et al[22] and is attributed to the presence of the short capillary segments in oligodendroglioma.[9] (Focally) elevated rCBV does therefore not necessarily indicate high-grade tumour in oligodendroglioma.

There is, however, a clear place for DSC perfusion imaging in the follow-up of oligodendroglioma. Even though baseline rCBV may be elevated in this compared with other low-grade glioma tumours, an increase in rCBV over time is indicative of malignant transformation. Such an increase can be seen up to 12 months before other signs of malignant transformation such as contrast enhancement, volume increase or clinical deterioration become apparent.[25] Furthermore, DSC perfusion imaging may be used to assess response to treatment and particularly to distinguish radiation necrosis from tumour progression. DSC perfusion imaging studies show low rCBV ratios in areas of radiation necrosis with reported thresholds of 0.6–0.7.[26,27] Sensitivity at these thresholds is >90% and specificity approaches 100%.[26] As with initial tumour staging, rCBV ratios are high in progressive tumour, with reported values of >2.6.[27]

K^{trans} can be estimated using MR steady-state dynamic contrast-enhanced perfusion imaging and is a combined measure of perfusion and capillary permeability. It assesses the leakage of contrast media through the vascular wall using T_1 weighted imaging. Again, multiple images of the same region of interest are acquired, for approximately 5–10 min. Correlation of K^{trans} with tumour grade is lower than that of rCBV, and it is more commonly used in the assessment of treatment effects. Although there is contrast enhancement, indicating mostly increased vascular permeability, in both radiation necrosis and recurrent tumour, enhancement is slow in radiation necrosis. K^{trans} is therefore low in areas of radiation necrosis.[19] As mentioned above, rCBV in these areas is also low, due to the lack of vascularization with radiation necrosis. Recurrent tumour, on the other hand, shows a rapid increase of contrast enhancement in the vascular phase, with correspondingly high K^{trans} values, followed by a steady leakage of contrast media. As mentioned above, rCBV in recurrent or progressive tumour is also high, owing to the presence of blood vessels as a result of neovascularization. These newly formed tumour vessels are poorly developed and thus very leaky, explaining the high K^{trans} values.

MR spectroscopy

MR spectroscopy is used to measure regional variations in neurochemistry and the concentration of various brain metabolites. Metabolites of interest are *N*-acetylaspartate (NAA), lactate and choline (Cho), as markers of neuronal and axonal density, anaerobic metabolism, and membrane synthesis and cellular density, respectively. Additionally, creatine (Cr), which is considered to be a relatively stable metabolite, is often used as an internal reference for calculating metabolite ratios. MR spectroscopy has a recognized role in oligodendroglioma tumour grading, especially where other imaging features such as contrast enhancement and rCBV fail to reliably predict tumour grade. The typical spectrum of oligodendroglioma shows moderately elevated Cho and decreased NAA without a lactate peak.[10] The absence of a lipid/lactate peak aids in differentiating oligodendroglioma from anaplastic oligodendroglioma.[10] Furthermore, a Cho/Cr ratio threshold of 2.33 was found to distinguish high- from low-grade oligodendroglioma with 100% sensitivity and 83% specificity.[28] Diagnostic accuracy may be further improved by using a multimodality approach, in which, for instance, perfusion imaging is used to guide the placement of regions of interest for MR spectroscopy measurement.[24]

For the distinction between radiation necrosis and recurrent tumour, a reduction of NAA, Cho, Cr with or without lactate/lipid peaks is reported to indicate radiation necrosis.[14] It has been postulated that a Cho/Cr or Cho/NAA ratio >1.8 indicates glioma tumour recurrence, but there is no consensus, as yet, on the measurements, ratios and method to use nor are there any reference values that are specific to (anaplastic) oligodendroglioma.[29]

Metabolic imaging (positron emission tomography)

Since the metabolic rate of oligodendroglioma correlates with its histological grade, there is considerable interest in visualizing tumour metabolism with PET. PET uses radioactively labelled tracers such as fluorine-18 fludeoxyglucose (^{18}F-FDG) and carbon-11 methionine (^{11}C-MET) to assess glucose and amino acid metabolism, respectively. Increased ^{18}F-FDG uptake is a fairly non-specific finding in malignant lesions and is due to the tumour cell's increased expression of glucose transport and glycolytic activity.[30] ^{18}F-FDG is, by far, the most commonly used tracer for clinical PET studies, but for the staging of primary brain tumours, a wide range of diagnostic accuracies has been reported, with some studies failing to correlate ^{18}F-FDG uptake with tumour grade. An added challenge with ^{18}F-FDG-PET is the avid uptake of ^{18}F-FDG by the grey matter, which is particularly problematic for the cortically localized oligodendroglioma.[30] ^{18}F-FDG-PET also seems to be of limited value for distinguishing tumour recurrence from radiation necrosis, especially in lesions treated with stereotactic radiosurgery. Reported sensitivity and specificity range from 81% to 86% and 40–94%, respectively.[30]

Better diagnostic accuracy may be obtained with amino acid metabolism tracers, of which ^{11}C-MET is the most commonly used. The main advantage of these tracers compared with ^{18}F-FDG is the low background activity in the normal brain parenchyma. ^{11}C-MET uptake is found to correlate with

several markers of tumour proliferation such as cell proliferation and microvessel density and is able to accurately distinguish high- from low-grade gliomas. ^{11}C-MET also distinguishes oligodendroglioma from astrocytoma, showing hypermetabolism in the former.[3] In the context of treatment monitoring, several studies have shown that ^{11}C-MET accurately detects tumour recurrence. However, there are also reports of similar diagnostic accuracy for distinguishing radiation necrosis from tumour recurrence with ^{18}F-FDG.[30]

Imaging features of 1p/19q codeletion

Several imaging features are more commonly seen in 1p/19q codeleted tumours, which may be used to distinguish these from 1p/19q intact tumours (Table 1).

Location

Codeleted tumours are most commonly located in the frontal, parietal or occipital lobes, whereas intact tumours are more likely to be found in the temporal, insular or temporoinsular region.[31,32] This was confirmed by Fellah et al[33] in their retrospective study of 50 WHO grade II–III oligodendroglioma and mixed oligoastrocytoma. 9 out of 19 codeleted tumours were found in the frontal lobe, but 9 out of 31 intact tumours were also located in the frontal lobe. On the other hand, 6 out of 19 codeleted tumours were found in the insular, albeit not temporoinsular, region, indicating the limited value of using location to distinguish between intact and codeleted tumours.

Appearance

Codeleted tumours generally have an indistinct tumour margin, have heterogeneous signal intensity on both T_1 weighted and T_2 weighted MRI, and commonly have the presence of calcifications (Figure 9).[32,34,35] Contrast enhancement does not generally distinguish between intact and codeleted tumours.[31,32] An indistinct tumour margin is also commonly seen in intact tumours and thus does not reliably distinguish between codeleted and intact tumours. A sharp tumour border, however, is only rarely seen in codeleted tumours and therefore makes a 1p/19q intact tumour more likely.[35,36]

Tissue heterogeneity is difficult to assess reliably with a subjective qualitative evaluation, resulting in large interrater variability and failure to detect differences between intact and codeleted tumours.[33] With texture analysis, however, signal intensity patterns are automatically quantified, and high sensitivity and specificity for this distinction can be obtained. Brown et al[37] showed that the mid-frequency domain of the T_2 weighted sequence differentiated codeleted from intact tumours with 93% accuracy. Sensitivity and specificity were much higher (93% and 92%, respectively) than those obtained with visual assessment (67% and 75%, respectively).

Susceptibility artefacts on MRI, presumably due to calcification as well as haemorrhage, have been reported to be more frequent in codeleted than in intact tumours, although they are common in both genotypes.[36] Conversely, several studies reported no significant difference in susceptibility artefacts,[32,35] and haemorrhage was only noted in WHO grade III tumours.[33]

Advanced and metabolic imaging

DSC perfusion imaging appears to be the most accurate technique to detect increased rCBV in the codeleted genotype.[38–42] This is presumably due to the microvascular proliferation present even in low-grade oligodendroglioma. An rCBV ratio of >1.6 was found to predict the codeleted genotype with 92% sensitivity and 76% specificity.[41] Histogram analysis is likely to be more accurate than the conventional hot-spot technique as shown by Emblem et al.[42] Not only were they able to identify codeleted tumours, they could also distinguish high- from low-grade gliomas (which included oligodendroglial tumours) and high- from low-grade oligodendroglial tumours.

MR spectroscopy and DWI seem to have limited value in distinguishing codeleted from intact tumours. Chawla et al[36] combined DSC MR perfusion imaging with MR spectroscopy by obtaining metabolite ratios from tumour regions with maximum rCBV. The Cho/Cr ratio was found to have the highest predictive value, but when combined with maximum rCBV, only a moderate accuracy of 69% was obtained. Lower maximum ADC and mean histogram ADC in codeleted tumours have been reported,[43] but others[33] found no ADC differences.

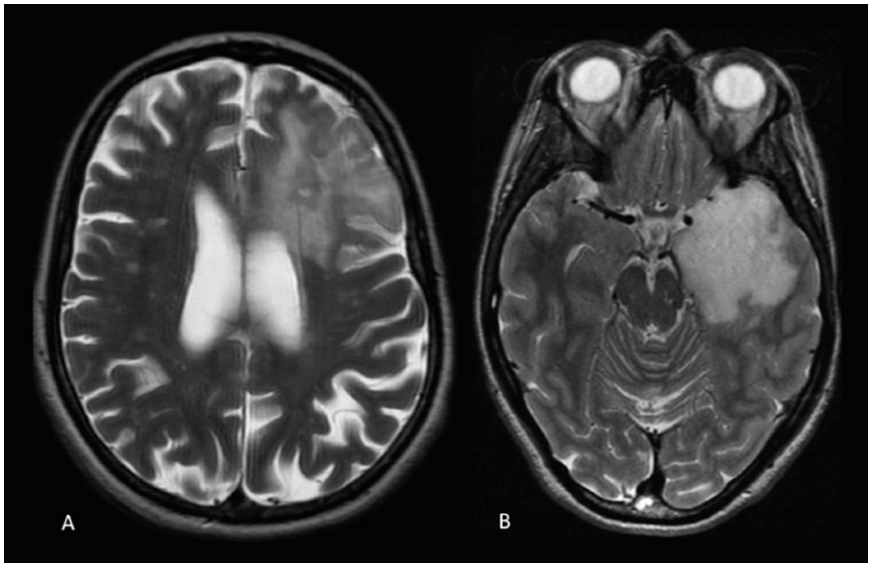
Codeleted tumours show increased uptake of ^{18}F-FDG, ^{11}C-MET and fluorine-18 fluoro-ethyl-tyrosine compared with intact

Table 1. Imaging features of 1p/19q intact *vs* codeleted oligodendroglioma

Imaging features	1p/19q intact	1p/19q codeletion
Location	Insular, temporal and temporoinsular	Frontal > parietal, occipital
Tumour margin	Commonly indistinct, but may be sharp	Indistinct
Calcifications	Uncommon (20%)	Common (>40%)
Signal intensity	Homogeneous	Heterogeneous (more on T_2 weighted than on T_1 weighted imaging)
ADC	Not different	Not different—lower maximum ADC
rCBV	Not increased in WHO grade II	Mildly increased in WHO grade II
^{18}F-FDG/^{11}C-MET/^{18}F-FET	Not increased	Mildly increased

ADC, apparent diffusion coefficient; ^{18}F-FDG, fluorine-18 fludeoxyglucose; ^{18}F-FET, fluorine-18 fluoro-ethyl-tyrosine; ^{11}C-MET, carbon-11 methionine; rCBV, relative cerebral blood volume; WHO, World Health Organization.

Figure 9. Transverse T_2 weighted sections of (a) 1p/19q codeleted tumour and (b) 1p/19q intact tumour. Note the heterogeneous signal intensity, indistinct border and frontal lobar location in the codeleted tumour (a). By contrast, the intact tumour is more homogeneous, has a relatively sharp tumour border and is located in the temporoinsular region (b).



low-grade tumours.[44–47] In high-grade tumours, however, no difference in ^{11}C-MET uptake was found between the genotypes.[47] In an unselected patient population, fluorine-18 fluoroethyl-tyrosine PET also failed to reliably predict the 1p/19q codeletion in the individual patient, mostly because of overlapping findings between oligodendroglial and high-grade astrocytic tumours.[46]

SUMMARY AND CONCLUSION

For the initial diagnosis of oligodendroglioma, MRI and CT are complementary; MRI is superior to CT in assessing tumour extent and cortical involvement, whereas CT is most sensitive to calcification. In contrast to other low-grade gliomas, oligodendroglioma may show enhancement after contrast administration. Anaplastic tumours do more commonly show contrast enhancement, as well as necrosis, haemorrhage and peritumoural oedema. None of these findings, however, are reliable features of high tumour grade.

Advanced and functional imaging techniques may aid in grading as well as in the differentiation between tumour recurrence and radiation necrosis, but so far, no unequivocal method or combination of methods is available. Despite a known inverse correlation between cellular density and ADC, DWI does not reliably distinguish low- from high-grade tumour. Elevated rCBV may be seen in low-grade tumours and cannot be used reliably for tumour grading. For the distinction between tumour recurrence and radiation necrosis, however, there is a clear place for perfusion imaging.

On MR spectroscopy, the absence of a lactate/lipid peak distinguishes oligodendroglioma from anaplastic oligodendroglioma. Elevated Cho/Cr and Cho/NAA ratios indicate tumour recurrence in the context of post-therapeutic changes. With metabolic PET imaging, ^{11}C-MET seems to outperform ^{18}F-FDG both for tumour grading and detection of tumour recurrence.

The imaging features of the 1p/19q codeleted genotype are those traditionally considered typical of oligodendroglioma: indistinct tumour margin, heterogeneous signal intensity and calcifications. The added value of advanced imaging techniques in distinguishing codeleted from intact tumours is modest, showing increased perfusion and metabolism in codeleted tumours. Accuracy is particularly low when both grade II and III tumours are considered, in which imaging features largely overlap. In these unselected populations, MR spectroscopy to assess the Cho/Cr ratio may be useful.

For initial diagnosis, both MRI and CT are indicated, and PET imaging may additionally be considered for tumour grading. For follow-up, MRI is the imaging modality of choice with a protocol including non-enhanced and contrast-enhanced T_1 weighted sequences, T_2 weighted and T_2 fluid-attenuated inversion recovery sequences, diffusion weighted and perfusion imaging, and MR spectroscopy upon indication.

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