**Radiological Diagnosis of Brain Tumours**

**Introduction**

This discussion case study explores the radiological diagnosis of brain tumours based on a fictitious case study of Mrs. Faradosa who had a personal history of breast cancer. This paper will provide a critical analysis of the diagnostic value, benefits and limitations of relevant imaging modalities for diagnosing brain tumours.

**Background**

Mrs. Faradosa who has been complaining of frequent headaches, increased intracranial pressure, vision disturbances, balance problems, facial paralysis, inability to concentrate, reduced memory, progressive confusion and numbness for about 6 weeks, was admitted following a partial seizure. The 45-year old female was previously diagnosed with early-stage breast cancer and successfully treated with radiotherapy, three years before she presented with the seizure. Having evaluated her breast cancer history and neurological deficits, the doctor suspected possible metastatic brain tumours and therefore, referred her to the radiological department for further diagnostic brain imaging studies.

**Brain tumours**

***Aetiology***

The aetiology of brain tumours has remained poorly understood because no clear causes have been proven by cancer research (Idowu & Idowu, 2008). However, the aetiology of brain tumours is only explained by a limited number of risk factors, especially personal or family history of cancers, exposure to neurocarcinogenic compounds and ionizing radiations to the head including untreated viral infections such as John Cunningham (JC) virus, cytomegalovirus, human immunodeficiency virus (HIV), simian virus 40 (SV-40), varicella-zoste and chicken pox (Idowu & Idowu, 2008; Pearce et al. 2012). There is consistent epidemiologic evidence that exposure to ionizing radiation to the head in childhood increases the risk of developing brain tumours later in adulthood. For instance, a cohort of children who underwent X-ray computed tomography (CT) scans to the head were demonstrated to have increased risk of developing brain tumours later in their adulthood in a radiation dose-dependent manner (Pearce et al. 2012). While brain tumours can be malignant (cancerous) or benign, they often result in life-threatening conditions, such as increased intracranial pressure, headaches, seizures, facial paralysis, memory problems, and coordination problems (Wilne et al. 2013).

Epidemiologic data from the Central Brain Tumour Registry of the United States (CBTRUS) indicate that only one third of brain tumours are malignant while the remaining two thirds are benign (Ostrom et al. 2014). The overall incidence rate of brain tumours and other tumours of the central nervous system (CNS) among adults (aged ≥20 years) is significantly higher in US than in the United Kingdom, estimated to be 27.9 and 6.8 per 100,000 persons, respectively (Cancerresearchuk.org, 2014; Ostrom et al. 2014). About 40% of patients with personal history of cancer of the lung, breast, skin, colon, pancreas, testes, ovary, cervix, renal cell carcinoma, and melanoma, have increased risk of developing brain metastases later in their lives (Fink & Fink, 2013; Purandare, 2011).

***Diagnosis***

The diagnosis of brain tumours is not straight forward, because histological or neurological characteristics of brain tumours often mimic other non-neoplastic neurological diseases such as stroke and multiple sclerosis among others (Omuro et al. 2006). Therefore, an objective diagnosis of brain tumours is a systematic process that requires thorough physical examinations, careful evaluation of patient clinical history and risk factors that may be indicative of possible brain tumours (Grant, 2004). Physicians usually suspect the possibility of primary or metastatic brain tumours in patients presenting with persistent corroborative symptoms, particularly increased intracranial pressure, unresolved headaches, seizures, facial paralysis, memory problems, and coordinating problems (Grant, 2004; Wilne et al. 2013).

Patients with known malignant tumours elsewhere in their bodies have increased risk of developing metastatic tumours in other parts of the body including the brain (Fink & Fink, 2013). However, at this stage, physicians usually recommend diagnostic imaging of the brain as a definitive diagnosis of brain tumours. CT scan and magnetic resonance imaging (MRI) scan are the most common diagnostic neuroimaging modalities used for diagnosing brain tumours noninvasively (Cancer Research UK, 2005; Fink & Fink, 2013). When available, MRI is preferentially used over CT for evaluating patients with suspected brain tumours owing to its putative sensitivity and specificity in detecting primary and metastatic tumours (Cancer Research UK, 2005). However, CT is still currently used for initial evaluation of patients presenting with neurological deficits in the emergency setting (Grant, 2004). Given that CT and MRI are complimentary neuroimaging techniques with both strengths and weaknesses, the choice of brain imaging modality for diagnosing suspected brain tumours should be informed by a diagnostic target to be achieved, emergency or non-emergency situation and the age of the patient (Cancer Research UK, 2005).

**Head CT scan**

CT scan of the brain has remained a routine imaging modality for diagnosing patients with suspected brain tumours owing to its availability and adequate technical capabilities to image bone and soft tissues including blood vessels at the same time (Fink & Fink, 2013). Owing to its availability and simplicity, acquisition of brain CT is much faster that MRI. This explains why CT scan is preferentially used for the emergency evaluation of patients presenting with acute neurological deficits characterised by dizziness, seizures or imbalances (Navi et al. 2013). A CT scan has technical capabilities of showing swelling, bleeding, and bone and tissue calcification and therefore, useful in detecting haemorrhagic brain lesions, which often occur due to increased vascularisation of primary brain tumours with numerous dilated thin-walled vessels or necrosis of brain tumours (Lieu et al. 1999; Sahni & Weinberger, 2007). Therefore, cranial CT scan can provide a differential diagnosis of haemorrhagic stroke and haemorrhagic brain tumour lesions (Sahni & Weinberger, 2007).

Importantly, a CT scan can show bone and tissue calcification and can also detect enlargement of intracranial fluid-filled spaces (ventricles) in the brain mass including changes in cranial bone and therefore, useful in diagnosing some types of brain tumours, especially those near or involving bone which may appear calcified or sclerotic (Mitsuya et al. 2011; Razek, 2011). It can also detect implantable devices without interacting with medical devices such as cardiac pacemakers, nerve stimulators and ferromagnetic vascular clips, which are known to exhibit magnetic properties (Porres et al. 2009). Therefore, a CT scan can be performed at no significant risk in patients with implantable medical devices (Hussein et al. 2014; Porres et al. 2009). CT images are free from motion artefacts owing to technical advances in CT image acquisition, which is less sensitive to motion interference due to patient movements and can be acquired rapidly. In addition, a CT can be performed in obese or claustrophobic patients (Bhowmik et al. 2012).

However, CT scans have important limitations worth highlighting. First, the non-contrast-enhanced CT, which is routinely used for initial evaluation of patients in the emergency setting, has very low sensitivity in detecting brain tumour lesions, especially those spatially located in the temporal lobe of the brain (Grant, 2004). Even the contrast-enhanced CT has low sensitivity in detecting tumours in the temporal lobe of the brain (Grant, 2004). Secondly, while contrast-enhanced CT scan can detect cerebral metastasis, it has low sensitivity in detecting multiple metastatic brain lesions (Purandare, 2011). Furthermore, contrast-enhanced CT has poor sensitivity and specificity in differentiating between tumour types such as low-grade gliomas, malignant gliomas and a brain metastasis (or metastases). Therefore, imaging findings on a CT scan can only be used as a “clinical guess” of the probable brain tumour to warrant further diagnostic imaging and brain tissue biopsy (Grant, 2004).

**Brain** [**MRI**](http://www.cancer.net/node/24578)

When available, MRI is increasingly being preferentially used for diagnosing patients with suspected brain tumours. Unlike CT scan which uses x-ray radiation, MRI uses strong magnetic fields with technical capabilities of providing detailed anatomical features, cellular structure, and microcirculation of brain tumours (Cancer Research UK, 2005). Brain MRI is currently considered a definitive imaging technique for the diagnosis and monitoring the response of brain tumours to cancer therapies. While CT scan is the routine imaging technique that can be used for initial diagnosis of brain tumours, MRI has enhanced sensitivity and specificity in delineating tumour types (malignant or benign) including tumour position and size (Cancer Research UK, 2005). The advantage of MRI is that it provides multimodal imaging options that enhance detection of anatomical and pathological changes of the brain that are indicative of brain tumours (Fink & Fink, 2013).

Dynamic contrast-enhanced MRI (DCE- MRI) is the mainstay of brain tumour diagnosis because it is useful evaluating microcirculation in malignant brain lesions (Gordon et al. 2014). In this case, T1- and T2 -weighted MR images can be enhanced using a contrast agent. Currently, the standard contrast agent is the gadolinium (Gd) because it can be readily administered to a patient intravenously and has better diffusion capacity to cross the blood-brain barrier (BBB) owing to its low-molecular weight. In Gd-enhanced T1-weighted MR images of the brain, the primary malignant brain tumours appear as hypo-intense dark areas while on Gd-enhanced T2-weighted images they appear as hyper-intense bright areas (Gordon et al. 2014). Numerous clinical studies have demonstrated that contrast-enhanced MRI is so sensitive that it can detect 2-3 times as many metastatic lesions (of less than 5mm in diameter) as contrast-enhanced CT. About 20% of patients diagnosed with solitary metastatic lesions on CT have actually multiple lesions when re-evaluated with contrast-enhanced MRI (Fink & Fink, 2013; Purandare, 2011).

While interpretation of Gd-enhanced T1- and T2-weighted MR images of the brain is the mainstay of brain tumour diagnosis (Gordon et al. 2014), this technique has important limitations worth highlighting. To start with, interpretation of Gd-enhanced T1- and T2- weighted MR images lacks technical capabilities of differentiating new from old tumour lesions or the non-tumoural ischaemic lesions. Furthermore, the two MRI imaging modalities lack technical capabilities of differentiating malignant from benign and high- from low-grade tumours (Fayed et al. 2008). However, the diagnostic limitations of Gd-enhanced T1- and T2-weighted MR images can be overcome by the use of diffusion-weighted imaging (DWI). With respect to brain tumour diagnosis, DWI-MRI modality is advantageous over T1- and T2-weighted MRI modalities, because it provides technical capabilities of distinguishing malignant from benign and tumoural from non-tumoural brain lesions (Gordon et al. 2014). However, the only limitation of DWI-MRI is that it lacks technical capabilities of distinguishing, types of brain tumours with low apparent diffusion coefficient (ADC) values. By this account, it is recommended that DWI-MRI be combined with T1- and T2-weighted or perfusion-weighted (PWI) MRI to enhance diagnostic accuracy of brain tumours (Fan et al. 2005).

While MRI is preferentially used for diagnosing brain tumours, patients with metallic implants such as pacemakers cannot enter MR space because of the known fatal interaction of MR signal with the metallic implants (Hussein et al. 2014; Porres et al. 2009). Unlike a CT scan, MRI lacks the technical capabilities of imaging bone of the skull and therefore, may not show bone calcification, calcified tumour matrix on the cranial bone, and the effects of brain tumours on the skull (Razek, 2011). It is however important to underscore that while MRI appears clinically useful in diagnosing suspected brain tumours, interpretation of CT/MRI scans do not definitively provide or accurately predict histological diagnosis of brain tumours (Grant, 2004). Therefore, while MRI scans provide the “best clinical guesses” of tumour types, accurate diagnosis of brain tumour types (glioma, low grade glioma, and metastases) requires histological confirmation of the brain tissue from biopsied from the tumour location (Grant, 2004; Purandare, 2011).

**Treatment options and prognosis**

The choice of a therapeutic strategy and patient pathway in treating brain tumours is influenced by tumour type, the anatomical position and pathological characteristics of the identified brain tumours (Grant, 2004). Tumours that are anatomically located outside the brain but within the skull can be surgically excised completely, with good prognostic outcomes (NICE, 2006; Grant, 2004). However, tumours that are anatomically located inside the brain mass are often difficult to be completely excised (National Institute for

Health and Clinical Excellence, 2006). However, such tumours can be treated with a combination of cranial radiotherapy and chemotherapy (NICE, 2006; Grant, 2004).

**Case presentation and analysis**

Mrs. Faradosa who clinically presented with partial seizure in the emergency department underwent immediate physical examination to establish her cardiac, neurologic and mental states according to pathways to diagnosing of brain tumours recommended by the UK’s NICE (2006). Based on her neurologic and mental deficits coupled with her previous breast cancer history (as a risk factor), the attending General Physician (GP) suspected that the patient could be having metastatic brain tumours and therefore, she was immediately evaluated by a non-contrast-enhanced CT. This was useful because CT was readily available and was rapidly performed in the emergency situation of the patient. A CT scan is recommended in the NICE guidelines as an initial evaluation of all patients presented with neurological deficits. The preliminary unenhanced CT revealed that the patient had hypodense lesions in the right hemispheric portion of her brain, therefore, confirming the presence of possible brain metastases. In this case, the patient was immediately referred by the GP to a neuroradiologist for further neurological examinations by neuroimaging. This step was also consistent with the NICE recommended pathways to diagnosing brain tumours. While in the hands of a neuroradiologist, the patient underwent contrast-enhanced CT to establish possibility of metastatic brain tumours, which revealed the presence of enhancing lesions surrounded by oedema located in the right hemispheric portion of her brain. However, given that contrast-enhanced CT frequently misses small lesions in multiple brain metastases (Fink & Fink, 2013), further diagnostic imaging was required to ensure all possible metastatic lesions are located. In this case, the patient was booked to undergo Gd-enhanced MRI.

Prior to Gd-enhanced MRI, the patient underwent pre-MR screening by a qualified, trained MRI specialist. The pre-MRI screening was important to ensure that the patient did not have biomedical implants and devices such as cardiac pacemakers known to fatally interact with MR signal to the disadvantage of the patient safety (Sawyer-Glover & Shellock, 2000). Based on the absence of history of medical implants/devices, the patient was deemed safe to enter the MR space where she underwent T1- and T2-weighted MRI before and after intravenous injection of 1 mmol/kg Gd-DTPA contrast agent. While unenhanced CT scan is capable of ruling out intracranial mass lesions, it has low sensitivity and specificity in detecting and differentiating malignant from benign tumours. Therefore, contrast-enhanced CT or an MRI was warranted to delineate the metastatic brain tumours. However, while contrast-enhanced CT could have detected metastatic brain lesions, it has low sensitivity in detecting multiple brain metastases. Now, given that the patient was suspected to have metastatic brain tumour lesions, the neuroradiologist was justified to employ the pre-contrast and post-contrast enhanced MRI. Contrast-enhanced MRI is highly sensitive than contrast enhanced CT in detecting small tumours, which is frequently missed on CT. In this case, the bimodal Gd-enhanced T1- and T2-weighted MRI revealed that the patient had two small ring-enhancing lesions located in the right and left hemispheric portions of her brain. However, the patient underwent supplemental DWI-MRI, because it was not yet clear whether the two lesions were truly malignant or benign. The DWI-MRI revealed that the metastatic brain lesions were truly malignant warranting brain tissue biopsies for histological confirmation. In this case, it is important to emphasise that while the diagnosis of possible brain tumours is first evaluated with head CT or MRI, brain tumours can be confirmed by surgical biopsy, which allows definitive histopathological classification. However, the feasibility of surgical biopsy may be lacking in few clinical cases (National Institute for Health and Clinical Excellence, 2006). In the present clinical case, the patient successfully underwent surgical biopsy which confirmed the metastatic tumour lesions.

**Conclusion**

The patient was thus diagnosed with metastatic brain tumours. Given that the identified metastatic lesions were anatomically located slightly outside the brain mass but within the skull, a team of neuroradiologist and neurosurgeons explored the plausibility of excision of the tumours. However, the tumours were not completely excised and therefore, the patient was treated with a combination of cranial radiotherapy and chemotherapy where she responded well.

**References**

Bhowmik, U., Zafar Iqbal, M., & Adhami, R. 2012, “Mitigating motion artifacts in FDK based 3D Cone-beam Brain Imaging System using markers”, *Central European Journal of Engineering,* Vol. 2, no. 3, pp.369-382.

Cancer Research UK, (2005). *MRI scan | Cancer Research UK*. [online] Available at: <http://www.cancerresearchuk.org/about-cancer/cancers-in-general/tests/mri-scan> [Accessed 5 Jan. 2015].

Fan, G., Zang, P., Jing, F., Wu, Z., & Guo, Q. 2005, “Usefulness of diffusion/perfusion-weighted MRI in rat gliomas: correlation with histopathology”, *Academic Radiology,* Vol. 12, no. 5, pp640-651.

Fayed, N., Davila, J., Medrano, J., & Olmos, S. 2008, “Malignancy assessment of brain tumours with magnetic resonance spectroscopy and dynamic susceptibility contrast MRI”, *European Journal of Radiology,* Vol. *67*, no. 3, pp.427-433.

Fink, K. R., & Fink, J. R. 2013, “Imaging of brain metastases”, *Surgical Neurology International,* Vol. 4, Supp 4, pp.s209-s219.

Gordon, Y., Partovi, S., Müller-Eschner, M., Amarteifio, E., Bäuerle, T., Weber, et al. 2014, “Dynamic contrast-enhanced magnetic resonance imaging: fundamentals and application to the evaluation of the peripheral perfusion”, *Cardiovascular Diagnosis and Therapy, Vol. 4*, no. 2, pp.147-164.

Grant, R. 2004, “Overview: brain tumour diagnosis and management/Royal College of Physicians guidelines”, *Journal of Neurology, Neurosurgery & Psychiatry,* Vol. *75*, Suppl 2, pp.ii18-ii23.

Hussein, A. A., Abutaleb, A., Jeudy, J., Phelan, T., Patel, R., Shkullaku, M. et al. 2014, “Safety of computed tomography in patients with cardiac rhythm management devices: assessment of the U.S. Food and Drug Administration advisory in clinical practice”, *Journal of the American College of Cardiology,* Vol. 63, no. 17, pp.1769-1775.

Idowu, O. E., & Idowu, M. A. 2008, “Environmental causes of childhood brain tumours”, *African Health Sciences,* Vol. *8*, no. 1, pp.1-4.

Lieu, A. S., Hwang, S. L., Howng, S. L., & Chai, C. Y. 1999, “Brain tumors with hemorrhage”, *Journal of the Formosan Medical Association,* Vol. 98, no. 5, pp.365-367.

Mitsuya, K., Nakasu, Y., Horiguchi, S., Harada, H., Nishimura, T., Yuen, S. et al. 2011, “Metastatic skull tumors: MRI features and a new conventional classification”, *Journal of Neuro-Oncology,* Vol. 104, no. 1, pp.239-245.

National Institute for Health and Clinical Excellence, 2006, “Improving outcomes for people with brain and other CNS tumours” the manual. London: National Institute for Health and Clinical Excellence (NICE). Guidance on Cancer Services. 2006

Navi, B. B., Kamel, H., Shah, M. P., Grossman, A. W., Wong, C., Poisson, S. N. et al. 2013, “The use of neuroimaging studies and neurological consultation to evaluate dizzy patients in the emergency department” *The Neurohospitalist,* Vol. *3*, no. 1, pp.7-14.

Obajimi, M. O., Ogbole, G. I., Adeniji-Sofoluwe, A. T., Adeleye, A. O., Elumelu, T. N., Oluwasola, A. O. et al., 2013, “Cranial computed tomographic findings in Nigerian women with metastatic breast cancer”, *Nigerian Medical Journal : Journal of the Nigeria Medical Association,* Vol. *54*, no. 2, pp.123-128.

Omuro, A. M., Leite, C. C., Mokhtari, K., & Delattre, J. Y. 2006, “Pitfalls in the diagnosis of brain tumours”, *Lancet Neurology, Vol. 5*, no. 11, pp.937-948.

Ostrom, Q. T., Gittleman, H., Liao, P., Rouse, C., Chen, Y., Dowling, J. et al. 2014, “CBTRUS statistical report: primary brain and central nervous system tumours diagnosed in the United States in 2007-2011”, *Neuro-Oncology, Vol. 16, Suppl 4*, pp1-63.

Pearce, M. S., Salotti, J. A., Little, M. P., McHugh, K., Lee, C., Kim, K. P. et al. 2012, “Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study”, *Lancet,* Vol. *380*, no. 9840, pp.499-505.

Porres , J. M., Cerezuela, J. L., Luque, O., & Marco, P. 2009 “Computed tomography scan and ICD interaction”, *Case Reports in Medicine,* Vol. 2009. 10.1155/2009/189429.

Purandare, N. C. 2011, “Inclusion of brain in FDG PET/CT scanning techniques in cancer patients: Does it obviate the need for dedicated brain imaging?” *Indian Journal of Nuclear Medicine: IJNM : The Official Journal of the Society of Nuclear Medicine, India,* Vol., *26*, no. 2, pp.64-66.

Razek, A. A. K. A. 2011, “Imaging appearance of bone tumors of the maxillofacial region”, *World Journal of Radiology,* Vol. *3*, no. 5, pp.125-134.

Sahni, R., & Weinberger, J. 2007, “Management of intracerebral hemorrhage”, *Vascular Health and Risk Management,* Vol. 3, no. 5, pp.701-709

Sawyer-Glover, A. M., & Shellock, F. G. 2000, “Pre-MRI procedure screening: recommendations and safety considerations for biomedical implants and devices”, *Journal of Magnetic Resonance Imaging, Vol. 12*, no. 1, pp.92-106.

Wilne, S. H., Dineen, R. A., Dommett, R. M., Chu, T. P. C., & Walker, D. A. 2013, “Identifying brain tumours in children and young adults” Vol. 347.