Journal of Medical Diagnostic Methods

Loong, J Med Diagn Meth 2012, 2:1
DOI; 10.4172/2168-9784.1000e106

Editorial Open Access

Emerging Trends in Oncology: Greater Role for Radiology

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Expanding Role of Radiology in Oncology

Interventional oncology is a rapidly emerging technology-driven subspecialty within radiology. Several notable therapeutic developments over the last few years offer patients hope in the fight against cancer, especially when conventional therapy has failed or is deemed unsuitable. Within the field of diagnostic radiology, functional imaging has also emerged as an essential tool in the fight against cancer, given its ability to predict tumour response earlier than anatomical imaging, as well as detect early recurrence.

Emerging Role of the Radiologist

Traditionally, radiologists have assumed a passive role when it comes to patient care. The radiologist reports the imaging study or performs an interventional procedure as requested by the clinician. A detailed understanding of the clinical situation leading to the radiologic investigation or intervention is often not known to the radiologist involved.

With increasingly complex clinical conditions being managed more aggressively, fuelled by the emergence of highly specialised imaging and therapeutic technologies, radiologists are now taking a more active role in patient management, functioning as equal partners in more instances. New imaging modalities and therapeutic options can be made available to the patients directly via the radiologist, often almost as soon as they appear in the market, as a result of direct radiologist to patient contact.

Percutaneous Tumour Ablation: Radiofrequency and Microwave Ablation

Surgery used to be the only means by which complete cure could be achieved in a cancer patient. Taking hepatocellular carcinoma as an example, interventional ablative procedures used to be reserved for patients deemed unsuitable for curative surgical resection, or for patients with disease recurrence [1]. However, percutaneous ablation of tumours is today recognized as potentially curative therapy for early hepatocellular carcinoma [2,3].

Radio Frequency Ablation (RFA) is the current standard of care in thermal ablation. In RFA, high frequency electrical currents are passed through an electrode which is percutaneously or intra-operatively placed within the tumour, creating heat which result in necrosis of tumour cells. However, this technique is limited by the overall size of the potential ablation zone. The maximum thermal ablation zones which can be created with radiofrequency ablation is about 4 cm. Accounting for the safety margins required for curative therapy, this limits the size of tumours which can be treated, usually taken as less than 3 cm [4,5]. Accurate targeting of the tumours is also critical, which can be difficult in some patients. Another consideration is the 'heat sink' effect [6,7]. When the tumour is being ablated is near a large vessel, for example, the inferior vena cava, the vessel acts as a 'heat sink' and can impair the adequate heating of adjacent tumour cells. This leads to inadequate therapy, with remnant disease at the edge of the ablation zone often being difficult to treat.

Several new technologies have been developed to overcome these deficiencies in RFA. One exciting new technology which we have incorporated into our clinical practice is the use of microwave in thermal ablative therapy. A microwave antenna is percutaneously placed in the centre of the tumour. The emitted electromagnetic waves agitate water molecules within the tumour, producing friction and heat, and induce cell death via coagulative necrosis. Consistently higher intratumoral temperatures, larger tumour ablation volumes and faster ablation times have been demonstrated [8]. The heat sink effect is also less in microwave when compared to radiofrequency ablation [8]. The ablation zones created by microwaves have been found to reach up to 7 cm [9-11], creating the opportunity to treat larger tumours percutaneously. Another advantage is shorter ablation times [12]. In our experience, satisfactory ablation is often achieved in less than 10 minutes as compared to about half an hour in radiofrequency ablation. This translates into better patient comfort, as well as decrease the need for prolonged sedation. Microwave technology potentially opens the doors to treating larger tumours, with greater patient tolerance and much less risk compared to surgery.

Cone Beam CT Scan in the Angiographic Suites

Another exciting field of development is imaging technology within the interventional suite. New imaging machines can assist in more accurate delivery of therapeutic agents. Regional chemotherapy involves administration of chemotherapeutic drugs directly to the arteries supplying blood the tumour. A higher dose of drug delivered to the tumour theoretically translates to increased cytotoxic effect. This has been demonstrated in pancreatic cancer, where dose dependent sensitivity of the tumour has been demonstrated.

The most common use of regional Trans-Arterial Chemo Embolisation (TACE) or radioembolization is in the treatment of primary and secondary hepatic malignancies. These take advantage of the dual blood supply to the liver. Most of the blood supply to hepatic tumours is via the hepatic artery, while that to normal liver parenchyma is via the portal vein. The arteries supplying the tumour are cannulated, with the desired position confirmed with conventional C-arm Digital Subtraction Angiography (DSA).

Tumour vascularity is traditionally identified by the presence of 'tumour blush' or abnormal neovascularity on conventional angiography. This can sometimes be difficult using a conventional DSA,

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Received December 10, 2012; **Accepted** December 12, 2012; **Published** January 17, 2013

Citation: Loong MTM (2013) Emerging Trends in Oncology: Greater Role for Radiology. J Med Diagn Meth 2: e106. doi:10.4172/2168-9784.1000e106

especially when superselective cannulation is required, or when there is complex vascular anatomy.

In Cone Beam CT (CBCT), the radiation source beam and flat panel detector are coupled together by a C-arm, and a volumetric dataset obtained with a single 180-degree rotation of the C-arm without moving the patient. The spatial resolution of a CBCT-acquired image is generally better than that of a Multi-Detector CT (MDCT) acquired image, while contrast resolution is better in MDCT systems [13]. CBCT-acquired images are useful in demonstrating more detailed vascular anatomical information that may not be shown on traditional DSA [14,15]. CBCT images can also more clearly demonstrate Lipiodol (and hence chemotherapeutic agent) retention within the tumour [13,16], allowing the interventional radiologist to better gauge treatment efficacy during the procedure itself.

The fact that CT angiography-like images can be obtained within the interventional suite with CBCT technology is a boon. As interventional radiologists become more involved in treatment of increasingly complex conditions, accurate depiction of tumour vascularity and assessment of accuracy of delivery of chemotherapeutic agents is absolutely essential.

The skull base which is an inherently difficult area to assess given its complex vascular anatomy, demonstrates how we have utilized CBCT technology in the evaluation of a skull base tumour. With conventional angiography, it was difficult to be certain that blood supply to the tumour was from the internal carotid artery. However, with CBCT-acquired images, further processed with multiplanar reconstructions, we were certain that blood supply was from the internal carotid artery. Chemotherapeutic agents were hence delivered via this artery. We have since evaluated all possible lesions with complex vascular anatomy with this new technology.

Role of Diagnostic Radiology in Interventional Oncology

Outside the interventional suite, functional Magnetic Resonance Imaging (MRI) has demonstrated great potential in the field of oncologic radiology. Traditionally, oncologic radiology has been based on anatomical imaging. Detection of tumour recurrence relies on the ability to identify masses which are sufficiently large, while response to therapy is based on change in tumour size. However, tumour response can occur in the absence of a change in size. Further, occasionally, increase in tumour size can actually indicate tumour response, such as the inflammatory changes which develop after thermal ablative therapy. The area of these inflammatory changes are often much larger than the size of the primary tumour. This makes the assessment of therapeutic efficacy difficult if one relies on size as the sole criteria.

Tumour response is absolutely critical in oncology, as this parameter is important in dictating further management. Decrease in tumour size after therapy may take up to 4 to 6 weeks and this is traditionally the earliest time at which follow up imaging is obtained to determine treatment efficacy. If one is able to predict tumour response early, one can alter chemotherapeutic regimes earlier, with the aim of achieving a better clinical outcome.

Functional MRI, namely Diffusion Weighted Imaging (DWI), offers the possibly of detecting changes in tumour cellularity early, which is an indicator of tumour response. DWI interrogates the motion of water molecules. In tissue, DWI signal is derived from movement of water molecules in the intra- and extracellular spaces, as well as the intravascular space [17]. As tumours generally demonstrate high cellularity, they usually have high DWI values [18]. If treatment is successful, loss of tumour cellularity occurs as the tumour becomes necrotic, leading to increased water molecular movement within the non-viable lesion [18,19]. This results in a decrease in the degree of restriction diffusion.

This technology has also proven useful in early assessment of tumour response post-therapy, including TACE of hepatocellular carcinoma [20,21] and metastatic hepatic nodules [22,23]. Not relying on change in tumour size to monitor response could pave the way to earlier changes in therapy, demonstrates a case of a liver metastatic nodule which we treated with TACE. 4 weeks post-therapy, while there was no change in size or signal characteristics on T1-weighted or T2-weighted imaging, loss of tumour cellularity was noted, as evidenced by loss of restricted diffusion with increasing signal on Apparent Diffusion Coefficient (ADC) imaging. Features were compatible with tumour response, even in the absence of change in anatomical dimensions. This case highlights how functional MRI can predict early treatment response, in the absence of a change in size, which conventionally is taken as tumour response.

Functional MRI has also been shown to be useful in monitoring therapy. It has also shown to be very useful in tumour detection [18]. DWI has been useful in imaging liver [24], prostate [25,26] and breast cancers [24], among others. Diffusion weighted imaging has shown potential in differentiating benign from malignant lesions [24]. In prostate cancer, specially tailored DWI sequences with ultra high b-value have been shown to improve the diagnostic accuracy of MR imaging [27]. DWI has also been shown to be a useful additional sequence in the detection of metastatic (e.g. nodal) deposits in oncologic imaging [28].

DWI is also useful in patients with allergy to MRI contrast or a history of significant renal impairment. Ever since the association of Nephrogenic Systemic Sclerosis (NSS) with Gadolinium-Based Contrast Agents (GBCA) was highlighted [29,30], there has been increasing reluctance to administer such agents to patients with impaired renal function. Since the use of intravenous contrast medium has traditionally been the mainstay of oncologic imaging in patients where use of GCBAs is cautioned, characterization of lesions can be difficult. In such cases, DWI imaging, a non-contrast based sequence, becomes extremely useful for the radiologist.

Summary

Radiology is making a great impact in the field of oncology, via both its therapeutic and diagnostic arms. This is related in no small part to emerging new technologies, several of which have been described in this article. It is thus the role of the radiology community to highlight the emergence of such technologies to the clinical community, and to the patients as well, given the increasing amount of direct patient contact today's interventional radiologist has.

With new technologies being developed at a steady rate, and the evolving role of radiologist, one can only envision the radiology community evolving into a force to be reckoned with, particularly in the field of oncology. Currently in developments are imaging modalities to detect molecular changes in cancer. These can potentially open the door for very early detection of cancer. Robotic or computed assisted devices are also now in development to aid the interventional radiologist in performing more and more complex and targeted therapy. The future is bright, we can dream of the day when all cancers can be detected at an early stage, and all can be treated with these minimally invasive techniques, leading to cancers being a disease which can be controlled, like a chronic ailment rather than a disease with high mortality.

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