Introduction

Malignant tumors are the second most common cause of death and are responsible for more than 12% of all deaths worldwide. Mortality rates and the success of therapeutic approaches depend mainly on the type of cancer, but they also depend on the presence of metastases. Therefore, tumor staging plays a key role for further treatment options in patients with malignant tumors. Since metastatic disease can affect different anatomic parts of the body, patients have to undergo several examinations, such as computed tomography (CT), magnetic resonance (MR) imaging, ultrasonography (US),scientigraphy, for staging of metastases. Thus, the staging process is often both time-consuming and expensive. Furthermore, the diagnostic accuracy remains limited (Van Den Brekel et al., 2000).

The high spatial resolution and excellent soft-tissue contrast make MR imaging an ideal tool for the detection of parenchymal and osseous lesions. The limited field of view restricting coverage to a single body region must be considered a major limitation of conventional MR imaging. Recently, whole-body MR imaging has been proposed for evaluation of the presence of metastases and/or for the evaluation of primary cancers (*O'Connell et al.*, 2002).

Some of the proposed whole-body MR imaging approaches either were limited by long acquisition times or provided only poor image quality owing to reduced spatial resolution and artifacts. Recently, fat saturated three dimensional (3D) gradient-echo sequences with nearly isotropic resolution have become available for parenchymal imaging (Walker et al., 2000).

Whole body MR imaging for the evaluation of metastases compared well with the reference techniques for cerebral, pulmonary, and hepatic lesions, whole body MR imaging was more sensitive in detection of hepatic and osseous metastases than were the reference techniques (*Lauenstein et al.*, 2004).

In comparison of whole body MRI with bone scintigraphy, whole body MRI was an excellent method for screening bone metastases especially vertebral bodies (*Schmidt et al.*, 2007).

Aim of the Work

Is to evaluate the role of whole-body MRI in detection of cancer metastases.

Metastatic disease, sometimes abbreviated mets, is the spread of a disease from one organ or part to another non-adjacent organ or part. Only malignant tumor cells and infections have the established capacity to metastasize (*Podsypanina et al.*, 2008).

Cancer cells can "break away", "leak", or "spill" from a primary tumor, enter lymphatic and blood vessels, circulate through the bloodstream, and settle down to grow within normal tissues elsewhere in the body. Most tumors and other neoplasms can metastasize, although in varying degrees (e.g., glioma and basal cell carcinoma rarely metastasize). When tumor cells metastasize, the new tumor is called a secondary or metastatic tumor, and its cells are like those in the original tumor. This means, for example, that, if breast cancer metastasizes to the lung, the secondary tumor is made up of abnormal breast cells, not of abnormal lung cells. The tumor in the lung is then called metastatic breast cancer, not lung cancer (*Klein*, 2008).



Fig. (1): Cut surface of a liver showing multiple metastatic nodules originating from pancreatic cancer (*Quoted from Klein*, 2008).



Fig. (2): Cut surface of a humerus showing a large cancerous metastasis (the whitish tumor between the head and the shaft of the bone) (*Quoted from Klein*, 2008).

Modes and sites of metastatic dispersal:

The most common places for the metastases to occur are the lungs, liver, brain, and the bones. There is also a propensity for certain tumors to seed in particular organs. This was first discussed as the "seed and soil" theory For example, prostate cancer usually metastasizes to the bones. In a similar manner, colon cancer has a tendency to metastasize to the liver. Stomach cancer often metastasizes to the ovary in women, then it is called a Krukenberg tumor. It is difficult for cancer cells to survive outside their region of origin, so in order to metastasize they must find a location with similar characteristics (*Chiang and Massagué*, 2008).

For example, breast tumor cells, which gather calcium ions from breast milk, metastasize to bone tissue, where they can gather calcium ions from bone. Malignant melanoma spreads to the brain, presumably because neural tissue and melanocytes arise from the same cell line in the embryo (*Klein*, 2008).

Cancer cells may spread to lymph nodes (regional lymph nodes) near the primary tumor. This is called nodal involvement, positive nodes, or regional disease. Localized spread to regional lymph nodes near the primary tumor is not

normally counted as metastasis, although this is a sign of worse prognosis. Transport through lymphatics is the most common pathway for the initial dissemination of carcinomas. In addition to the above routes, metastasis may occur by direct seeding, e.g., in the peritoneal cavity or pleural cavity (*Klein*, 2008).

Metastasis and primary cancer:

It is theorized that metastasis always coincides with a primary cancer, and, as such, is a tumor that started from a cancer cell or cells in another part of the body. However, over 10% of patients presenting to oncology units will have metastases without a primary tumor found. In these cases, doctors refer to the primary tumor as "unknown" or "occult," and the patient is said to have cancer of unknown primary origin (CUP) or Unknown Primary Tumors (UPT). It is estimated that 3% of all cancers are of unknown primary origin. Studies have shown that, if simple questioning does not reveal the cancer's source (coughing up blood-'probably lung', urinating blood-'probably bladder'), complex imaging will not either. In some of these cases a primary may appear later (*Yoshida et al.*, 2000).

The use of immunohistochemistry has permitted pathologists to give an identity to many of these metastases. However, imaging of the indicated area only occasionally reveals a primary. In rare cases (e.g., of melanoma), no primary tumor is found, even on autopsy. It is therefore thought that

some primary tumors can regress completely, but leave their metastases behind (Yoshida et al., 2000).

Common sites of origin:

- Lung.
- Breast.
- Skin: Melanoma (other skin tumors rarely metastasize).
- Colon.
- Kidney.
- Prostate.
- Pancreas

Symptoms

The symptoms of metastasis varies with location of the tumors. Initially, nearby lymph nodes are struck early. Lungs, bones, liver, and brain are the most common metastasis locations from solid tumors.

- In lymph nodes, a common symptom is lymphadenopathy.
- Lungs: cough, hemoptysis and dyspnea (shortness of breath).
- Liver: hepatomegaly (enlarged liver) and jaundice.
- Bones: bone pain, fracture of affected bones.

■ Brain: neurological symptoms such as headaches, seizures, and vertigo (*Briasoulis and Pavlidis*, 1997).

Although advanced cancer may cause pain, it is often not the first symptom. Some patients, however, don't show any symptoms (Fig. 3) (*Briasoulis and Pavlidis*, 1997).

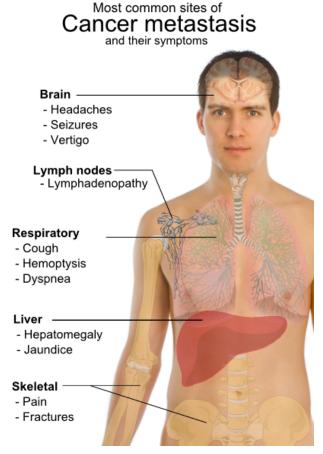


Fig. (3): Symptoms of cancer metastasis depend location of the tumor (Quoted from Briasoulis and Pavlidis, 1997).

Primary and secondary tumors:

The cells in a metastatic tumor resemble those in the primary tumor. Once the cancerous tissue is examined under a microscope to determine the cell type, a doctor can usually tell whether that type of cell is normally found in the part of the body from which the tissue sample was taken.

For instance, breast cancer cells look the same whether they are found in the breast or have spread to another part of the body. So, if a tissue sample taken from a tumor in the lung contains cells that look like breast cells, the doctor determines that the lung tumor is a secondary tumor. Still, the determination of the primary tumor can often be very difficult, and the pathologist may have to use several adjuvant techniques, such as immunohistochemistry, FISH (fluorescent in situ hybridization), and others. Despite the use of techniques, in some cases the primary tumor remains unidentified (*Sokoloff et al.*, 2000).

Metastatic cancers may be found at the same time as the primary tumor, or months or years later. When a second tumor is found in a patient that has been treated for cancer in the past, it is more often a metastasis than another primary tumor(Sokoloff et al., 2000).

How cancer spread:

Metastases takes place in many ways: through the lymphatic system, through the bloodstream, by spreading through body spaces such as the bronchi or abdominal cavity, or through implantation. The most common way for cancer to spread is through the lymphatic system. This process is called "embolization". The lymph system has its own channels that circulate throughout the body, similar to the veins and arteries of the bloodstream. These channel are very small and carry a tissue fluid called lymph throughout the body (*Klein*, 2008).

Often when a solid tumor is removed by surgery, the surgeon will remove not only the tumor but the neighboring lymph glands, even though there is no visible sign of cancer in those glands. This is done as a precautionary measure, because if even one cell has broken away from the tumor and lodged in the lymphatic system, the cancer could continue growing and metastasizing. Cancer can also metastasize through the bloodstream. Cancer cells, like healthy cells, must have a blood supply in order to live, so all cancer cells have access to the bloodstream. Malignant cells can break off from the tumor and travel through the bloodstream until they find a suitable place to start forming a new tumor. (Tumors almost always metastasize through the veins rather than through the arteries). Sarcomas

spread through the bloodstream, as do certain types of carcinomas, like carcinoma of the kidneys, testicular carcinoma, and Wilms' tumor, a type of kidney cancer seen in young children. Cancers may spread by more than one route (*Weidner et al.*, 1991).

Cancers can also spread by local invasion that is, by intruding on the healthy tissue that surrounds the tumor. Some cancers that spread this way do not venture very far from the original site. An example of this kind of cancer is basal cell carcinoma of the skin. When this kind of cancer is removed by surgeon, a wide area of healthy tissue surrounding it is also removed and it is usually "cured" immediately. Unless some cells have been left behind, it is very unlikely that it will recur. (However, it is possible that a second cancer of the same kind may start to grow at a later time at a completely different site the new growth having nothing to do with the first) (*Yoshida et al.*,2000).

A very rare type of metastasis is caused by implantation or inoculation. This can happen accidentally when a biopsy is done or when cancer surgery is performed. In this case malignant cells may actually drip from a needle or an instrument (this is also called a "spill"). It is desirable, therefore, if possible and if the cancer is small to remove it

completely at the initial surgery that is at the time of the biopsy. Cancers do not spread in a completely random fashion. Some parts of the body are more vulnerable to becoming metastatic sites than others. For example cancers rarely metastasize to the skin, but they often metastasize to the liver and lungs. Each type of cancer has its own pattern for metastases (*Podsypanina et al.*, 2008).

Basic Physics of MRI

MR describes the phenomenon whereby the nuclei of certain atoms, when placed in a magnetic field, absorb and emit energy of a specific frequency. The spectrum of absorbed or emitted energy depends upon the nucleus under observation and its chemical environment. Nuclei suitable for MRI are those which have an odd number of protons or neutrons and therefore possess a net charge and have angular momentum. Because of the combination of charge and angular momentum, these nuclei behave as magnetic dipoles. Almost all images produced to date have been of the nuclear magnetism of the hydrogen nucleus (or proton) which is a particularly favourable nucleus from the MRI standpoint, and is present in virtually all biological material. Other naturally occurring magnetic nuclei which are of interest include phosphorus (³¹P), sodium (²³Na), carbon (13C) and potassium (39K). In addition, exogenous noble gases such as helium (³He) and xenon (¹²⁹Xe) can be made sufficiently sensitive by polarization outside the magnet using laser techniques to allow imaging of airways and in the case of xenon, blood perfusion. The proton can be regarded as if small, freely suspended bar magnet spinning rapidly about its magnetic axis. When a group of protons is placed in a uniform magnetic field, their magnetic field and moments experience a

couple tending to turn them parallel to the direction of the field (*Paley et al.*, 2001).

In a strong magnetic field, more of these nuclear magnetic dipoles align with the applied static magnetic field than against it. This produces a net magnetization in the direction of the field. The direction of the strong magnetic field conventionally defines the z axis, which is generally along the longitudinal axis of the patient in a typical MRI imaging machine. In an interventional open magnet the field is often in the vertical direction. In dedicated extremity and neonatal MR the field is in the horizontal plane across the magnet. The strong magnetic field, which must be homogeneous over a volume large enough to contain the human body in an MRI imaging machine. is provided by a resistive, permanent superconducting magnet. Magnetic field strengths used for clinical imaging currently range from 0.02 Tesla (T) to 8 T (Paley et al., 2001).

Because the nuclei are spinning, they respond to the magnetic couple with their axes are tilted so that they come to rotate at exactly the same frequency about the magnetic field; direction in a movement known as 'precession'. The frequency of precession is directly proportional to the applied magnetic field for protons in a field of 1 T, it is 42.6 MHz. This