INTRODUCTION AND AIM OF WORK

The bone marrow is the largest organ of the body by weight next to bones, muscles and fat. It's function is to provide a continuous supply of red cells and platelets and white cells to meet the body's demands for oxygenation, coagulation and immunity *(Vogler and Murphy, 1988)*.

The study of bone marrow abnormalities is taken in this thesis by conventional plain film radiology, radionuclide scintigraphy and computed tomography as well as MRI examination .

Accurate diagnosis of different bone marrow lesions is important to assess the disease stage as in lymphoma in order to imply the best treatment protocol according to it *(Varan et al., 1999).*

Combination of some or all diagnostic methods such as clinical ,imaging, histological and biochemical information is essential to bring out the correct diagnosis to each disease *(Steiner et al., 1993)*.

Namely, the MRI has acquired an increasingly important role in evaluation of bone marrow lesions as it the best known modality of choice in discrimination between normal and abnormal bone marrow and in featuring the surrounding tissues *(Steiner et al., 1993)*.

The aim of this work is to discuss the role of different radiological and imaging modalities in diagnosis of bone marrow lesions.

STRUCTURE, FUNCTION AND DISTRIBUTION OF BONE MARROW

Within the confines of the human skeleton lies one of the largest and most important organs of the body, the bone marrow. Its function is to provide a continual supply of erythrocytes, platelets and leukocytes in response to body's needs for oxygenation, coagulation and immunity *(Vogler and Murphy, 1988)*.

Haematopoiesis: is the process of blood cell production. Prior to birth, this process is confined exclusively to the yolk sac, which remains the source of haematopoiesis until the sixth week of intrauterine life. From the sixth to the twentieth week, the reticuloendothelial system and the liver are the primary sites for blood cell formation. During the late second trimester, the source of blood cell production is the bone marrow, which remains the primary site for blood cell synthesis through out life *(Abboud and Lichtman, 1995).*

Sustaiend cellular production is dependent on stem cells, which exhibit properties of both continuous self-replication and differentiation into specific cell lines *(Stoller et al., 1997).*

Stem cells differentiate into the erythroid, granulocyte, monocyte, thrombocyte, and lymphoid

cells which further differentiate to form erythroblasts, myeloblasts, macrophages, platelets and T-and B-lymphocytes. Stem cells are found in the peripheral blood, as well as, the bone marrow. Disorders of stem cells are responsible for many diseases *(Kaplan and Dussault, 1997 and Steiner et al., 1992).*

Types of bone marrow: There are two types of bone marrow, red and yellow marrow .

Red marrow also called the active or cellular marrow ,is semi-fluid in consistency and is composed of the various hematopoietic cells that include erythrocytes, granulocytes and thrombocytes as well as lymphoid nodules. The cellular elements are supported by reticulum and fat cells. Red marrow contains approximately 40% water, 40% fat, and 20% protein. Concentrations of red marrow in the adult persist primarily in the spine, pelvis, scapulae, sternum, ribs, skull, and proximal metaphysis of humeri and femora. (Figure 1). The distribution of red marrow remains the same throughout life, once the mature pattern of marrow distribution is achieved. However, the fraction of red marrow in the proximal long bones and axial skeleton decreases with age, and is replaced by increasing amounts of fat cells *(Moore and Sebag, 1990).*

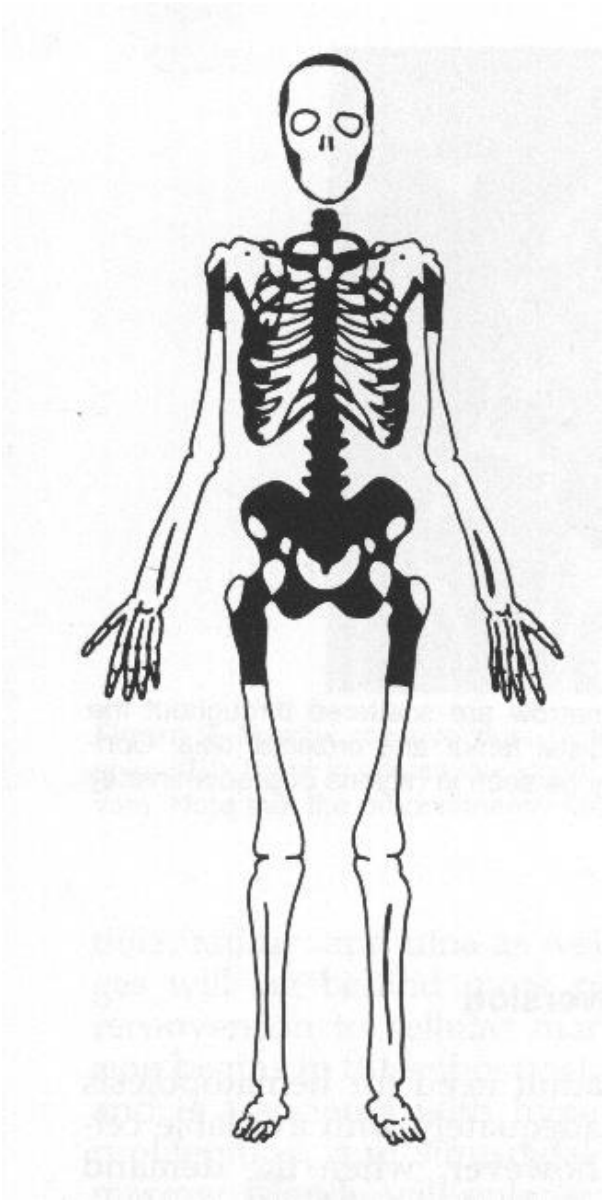

Figure 1: Normal distribution of adult marrow. Macroscopic red marrow resides in the vertebral bodies, flat bones, and proximal metaphysis of the femora and humeri (shaded areas). The remainder of the skeleton (white areas) contains primarily yellow marrow *(Quoted from Moore et al., 1991).*

Yellow marrow also called inactive or fatty marrow, is the part of marrow not involved in blood cell production. The function of which has not been definitely established .Still they provide surface and nutritional support. It is predominantly composed of fat. It contains approximately 15% water. 80% fat, and 5% protein. It predominates in the rest of appendicular skeleton as seen in (Figure 1) *(Vogler and Murphy, 1988).*

The vascular supply of bone marrow consists of centrally located nutrient arteries that send branches which terminate in capillary beds within the bone marrow cavity. Post-capillary venules coalesce to form venous sinuses. The sinusoids drain into the central venous sinus of the medullary canal, which then exits through the nutrient foramen. Hematopoietic cell production follows the vascular arrangement, forming active hematopoietic islands between the sinusoids. Bone marrow lacks lymphatic channels while bone marrow nerve supply follows a similar course to the arterial supply *(Vogler and Murphy, 1988).*

Bone marrow conversion and reconversion:

Normal physiologic conversion of red to yellow marrow occurs gradually and progressively during

growth in a predictable and orderly fashion *(Weinreb, 1990).*

This process of marrow conversion occurs from the periphery to the center but at different rates in different bones and at different sites within each bone. It begins within the terminal phalanges of the hands and feet shortly before birth, and proceeds throughout childhood and adolescence, initially involving distal bones and subsequently progressing to more proximal portions of the appendicular skeleton. In individual long bones, conversion occurs first in the diaphysis, then in the distal metaphysis, and finally in the proximal metaphysis *(Mirowitz, 1993 and Jaramillo et al., 1991).*

Conversion proceeds from the appendicular to the axial skeleton in a roughly symmetric manner from birth to mid-twenties. In the appendicular skeleton, the distal bones of the feet and hands, lower legs, and forearms undergo conversion prior to the femora and humeri. *(Ricci et al., 1990 and Duda et al ,1995).*

Reconversion of yellow to red marrow :

When the demand for hematopoiesis is elevated because of replacement or destrubtion of normal cellular marrow or because of hemolysis, reconversion from fatty to cellular marrow takes place *(Guckel et al., 1990).*

Reconversion of yellow to red marrow occurs in the reverse order from that seen in the normal, physiologically maturing skeleton. In other words, it starts in the axial skeleton and then proceeds in a proximal-to-distal direction in the appendicular skeleton (first in the proximal, then in the distal metaphyses, followed by the diaphysis) *(Ishijima et al., 1996 and Kaplan et al., 1992).*

Some factors that have been associated with marrow reconversion; includes smoking, obesity, anorexia and prolonged immobilization *(Babyn et al., 1998 and Rao et al., 1988).*

APPEARANCE OF NORMAL MARROW

A variety of radiologic techniques are currently available for assessing bone marrow, including conventional radiography, CT, radioactive isotopic scanning and MRI.

Conventional radiography: On plain X-ray calcified portions of growing bones cast opaque shadows of calcium density, non calcified components cast shadows of lesser density comparable to that of other non calcified tissues apart from fat. The overall density of a bone is provided almost exclusively by the cortical bone. Channels for nutrient vessels may present as focal defects in specific areas. Several changes of appearances of bones on X-ray as （increase in length, fusion, decreased density ）occurs with different ages (Figure 2)*(Silverman and Kuhn, 1993).*

On computed tomography (CT images) : CT cannot distinguish hematopoietic marrow from fatty marrow. The examined tissues absorb the X-ray beam from the CT machine to various degrees depending on the anatomic number and density of specific tissue. The remainder of X-ray which is not absorbed passes through the tissue and is detected and processed by the computer. The CT computer soft ware converts the X-

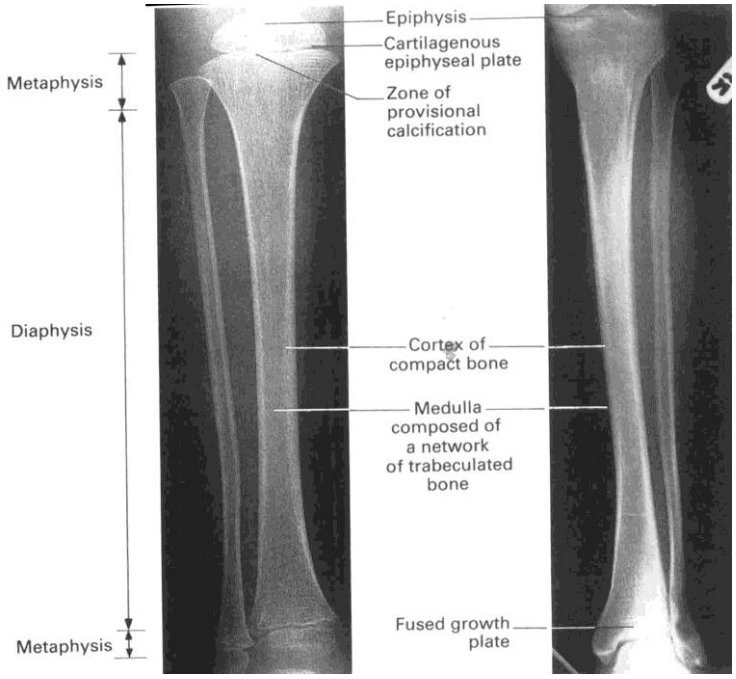

Figure 2: Plain X ray of a normal long bones in a child and adult in AP projection illustrating different parts seen by x-ray *(Quoted from Silverman and Kuhn,1993)*

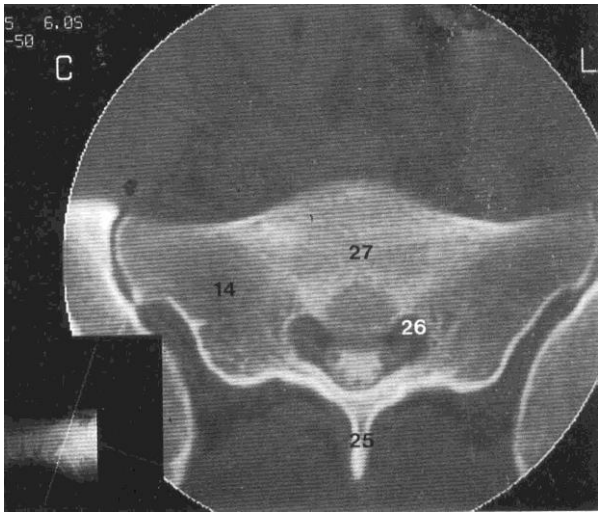

Figure 3: Axial CT images at level of sacrum with intrathecal contrast injection showing different parts of it *(Quoted from Weir et al., 1997).*

ray beam attenuations of the tissues into a CT number (Hounsfield units) by comparing it with attenuation of water. This accounts for appearance of different tissues. The HU of water is 0, of air is – 1000 and of normal cortical bone + 1000 so it appear with great density (Figure 3) *(Greenspan,2000).*

Magnetic resonance imaging (MRI) pulse *sequences:* The pulse sequence used influences the MRI appearance of bone marrow:

Spin-echo and fast spin-echo (FSE) sequences:

Conventional T1- and T2 weighted spin-echo (SE) sequences remain the main stay of clinical MR marrow imaging. In most cases, the difference in T1 and T2 relaxation times allows the differentiation of normal red marrow from normal yellow marrow and from pathologic marrow *(Babyn et al., 1998).*. In a T1-weighted spin-echo sequence a short TR between 400 and 700 msec and short TE less than 30 msec is used for marrow characterization. On T2 weighted spin echo a long TR and long TE is used *(Delfaut et al, 1999).*

On T1-weighted and conventional T2-weighted spin echo MR images, yellow marrow demonstrates hyperintense signal intensity similar to that of subcutaneous fat. This is because the abundance of hydrogen protons in the CH_2 side chains of fat causes

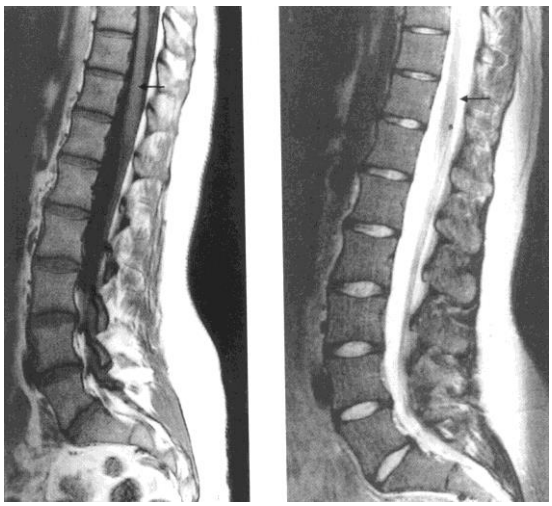

Figure 4: Normal marrow. A-Sagittal T1W images of lumbosacral spine shows intermediate signal red marrow through out vertebral bodies that is slightly higher than the discs. B-Sagittal T2WI's.The discs and CSF appear as high signal *(Quoted from Armstrong et al., 2004).*

A B

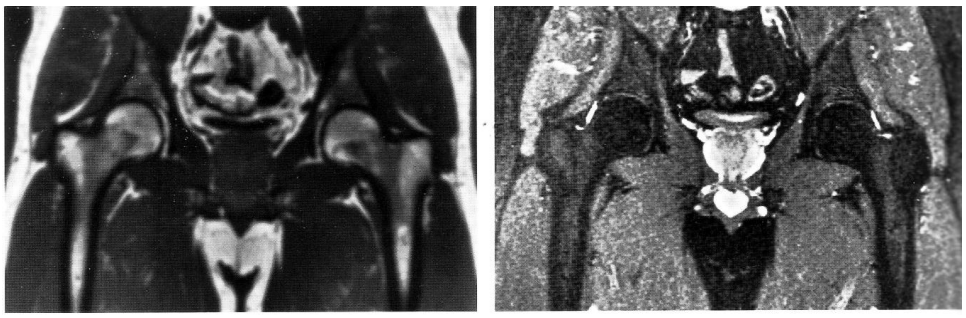

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Figure 5: Normal marrow: A- T1W image&B-STIR : Coronal images of the pelvis and hips. Red marrow is higher than muscles on T1 & similar to it on STIR localized in metaphysis and pelvis. Fatty marrow is in epiphysis &diaphysis with high signal on T1 &low signal on STIR images *(Kaplan and Dussault, 1997).*

high signal intensity on MRI identical to subcutaneous fat *(Bushberg et al., 1994).*

The signal intensity of fatty marrow is slightly decreased on conventional T2-weighted images compared to T1-weighted images, resulting in decreased contrast between yellow and cellular marrow when compared with T1-wiehgted images.*(Stoller et al., 1997).*

On T1-weighted images, the signal intensity of red marrow is considerably less than that of fatty marrow due to its increased cellularity. Unless red marrow is extremely hypercellular, as normally seen only in infants, its signal on T1-weighted images should be of intermediate intensity greater than that of adjacent muscle or non-degenerated intervertebral discs.(Figures 4 & 5) On T2-weighted sequences, the signal intensity of red marrow usually shows a small increase, becoming slightly brighter than muscle and approximating the signal intensity of fatty marrow. (Figure 4) Other factors; such as iron content and microscopic fat droplets within red marrow stores, contribute to its overall signal intensity *(Stoller et al., 1997).*

Fast T2-weighted spin-echo imaging has largely replaced conventional T2-weighted spin echo imaging Normal fatty marrow shows a higher signal intensity

on fast spin echo T2-weighted images when compared with conventional T2-weighted spin echo images (*Caldemeyer et al, 1996).*

Short time inversion recovery (STIR)

The STIR sequence is a fat-suppression technique, which is helpful in increasing the conspicuity of marrow lesions, STIR imaging uses a 180°C inversion pulse to invert all tissue protons *(Moulopoulos and Dimopoulus, 1997).*

Fat suppression should enable simultaneous assessment of the osseous and soft tissue components of musculo skeletal lesions, both of which are not optimally depicted on either T1-weighted or T2-weighted images. So fat suppression contributes to image quality by reducing the fat induced motion *(Peterfy et al., 1994).*

On STIR images, fat is black(Figure 5), combination of red and yellow marrow are of intermediate signal intensity, and most marrow tumors are of bright signal. Fibrous tissue, calcification, and hemosiderin deposits are low in signal intensity, whereas fluid, edema, or recent hemorrhage are all bright. Muscles remain intermediate in signal intensity as the marrow signal (Figure 5) *(Arndt et al., 1996 and Mirowitz et al., 1994).*

MR APPEARANCE OF RED TO YELLOW MARROW CONVERSION

Skull

The skull is an especially difficult area to evaluate as normal haematopoietic activity continues into adulthood. It is also where the bone marrow is most frequently imaged by MR in childhood, often incidentally in studies of the brain *(Simonson and Kao, 1992).*

There are three patterns of marrow distribution in the skull as seen in T1W sequence :

- **Pattern 1**: is characterized by bone marrow of uniformly low signal intensity or, at most, the presence of very small areas of high signal intensity in frontal and occipital bones.
- **Pattern 2**: frontal and occipital bones have uniformly high signal intensity, and patchy areas of high intensity appear in the parietal bone.
- **Pattern 3**: the entire skull has uniformly high signal intensity.

Pattern 1 is found predominantly in the patients younger than 10 years.
Pattern 2 and 3 have a relatively unfirom distribution with age *(Ricci et al., 1990).*