The Egyptian Journal of Hospital Medicine (July 2017) Vol.68 (2), Page 1260-1271

The Diagnostic Value of Combined Conventional MRI and Diffusion Weighted MRI in Diagnosis of Non-Palpable Undescended Testes

Aisha Dabnon Abd Alnabie
Faculty of Medicine, Ain Shams University

ABSTRACT

Background: MRI is noninvasive imaging tool, does not involve ionizing radiation and yields multiplanar images but it is sometimes less efficient in locating intra-abdominal functioning testicles and it fails to locate most of the atrophied testicles. Additional MRI assessments, as fat-suppressed T2WI and DWI are useful methods to improve the accuracy and sensitivity of diagnosis of non-palpable testes.

Objective of the Study: is to assess the value of adding diffusion-weighted sequences (DWI) to routine magnetic resonance imaging (MRI) in identifying and locating nonpalpable undescended testes.

Results: a combination of DWI and conventional MRI including Fat-supp. T2WI sequence is the most accurate means of detecting and localizing non-palpable undescended testes. The findings of DWI complement the information on the location of undescended testes obtained with conventional MRI. In addition, DWI is helpful in detection of testicular viability or atrophy properly before the operation.

Keywords: magnetic resonance imaging; undescended testes, diffusion, fat-suppression T2WI.

INTRODUCTION

Undescended testis or cryptorchidism, a condition in which one or both testicles are not appropriately positioned in the scrotum at birth. It is the most common congenital genitourinary anomaly in boys and has an incidence of 1–3% in term and 15–30% in premature male infants. approximately 20% of undescended testes are nonpalpable and either located in the abdomen or the canaliculi, or atrophic or are completely absent. Cryptorchidism is associated with impaired fertility, inguinal hernia, and increased risk of testis cancer [(1)].

The Preoperative identification and location of testicles can help to determine the optimal type of procedure and allow for appropriate advance planning. On the basis of the imaging findings, the surgeon can appropriately counsel the patient and alter the operative approaches needed. The imaging findings could obviate the need for surgical exploration.in the case of absent or vanishing testicles [(2)].

The Various imaging techniques have been suggested for use in identifying and locating non-palpable testicles preoperatively with varying limitations including expense, invasiveness technical difficulty, radiation risk, need for contrast medium, and need for sedation. Imaging approaches include ultrasonography, computed tomography (CT), routine MRI, magnetic resonance angiography (MRA), and magnetic resonance venography (MRV), some of which require sedation or anesthesia and are without risks [(3)].

The least expensive and frequently used technique of all imaging tools is ultrasound. However, it had been shown to have low sensitivity in identifying non-palpable testicles preoperatively in a recent meta-analysis [(4)].

Conventional MRI is moderately specific in identifying absent testicles but poorly sensitive in identifying the presence of non-palpable testicles. Conventional MRI appears to be less efficient in locating intra-abdominal functioning testicles and shows limited sensitivity in locating inguinoscrotal testicles, but it fails to locate most of the atrophied testicles, which makes conventional MRI a less reliable technique in providing guidance to differentiate those children needing surgery from those who do not [(5)].

Additional MRI assessments, fat-suppressed T2WI and DWI are useful methods to improve the accuracy of diagnosis of non-palpable testes. It could prevent needless surgery and be worth the additional imaging tests [(6)].

Diffusion weighted imaging (DWI) is an evolving technology with the potential to improve tissue characterization when findings are interpreted in conjunction with findings obtained with other conventional MRI sequences. It provides functional and structural information about biologic tissues; it is best used to solve specific problems [(7)]. Use of DWI therefore facilitates characterization of tissue at the microscopic level in a mechanism different from T1 and T2 relaxation. The degree of restriction of water diffusion in biologic tissue is inversely related to tissue cellularity and the integrity of cell membranes (e.g. tumor tissue). Concordantly, intra-abdominal

Received:7 / 5 /2017
Accepted: 16/ 5/2017
DOI : 10.12816/0039059

testes are considerably more cellular than the adjacent organs and tissues and can be detected easily on DW images owing to their increased signal intensity. Therefore, added DWI to routine MRI to identify non-palpable undescended testes [8].

Embryology and Anatomy of the Male Genital Organs

The chromosomal basis for sex is determined at conception. The internal and external genital structures still undifferentiated for up to 6 weeks gestation. Three important precursor components of the genital system are the genital ridge, the germ cells, and the two sets of internal sex ducts, namely, the müllerian-paramesonephric ducts and the wölffian-mesonephric ducts [9].

✓ **Development of Testes**

If an embryo is genetically male, the primordial germ cells carry an XY sex chromosome complex. Under effect of the SRY gene on the Y chromosome, which encodes the testis-determining factor, the primitive sex cords continue to proliferate and perforate deep into the medulla to form the testis or medullary cords. In the fourth month, Testis cords are composed of the primitive germ cells and the sustentacular cells of Sertoli originate from the surface epithelium of the gland [10].

Interstitial cells of Leydig, derived from the original mesenchyme of the gonadal ridge, lie between the testis cords. They begin the production of testosterone, and the testis is able to influence sexual differentiation of the genital ducts and external genitalia during 3rd and 4th months of gestation [10].

Testis cords remain solid until puberty, they join the rete testis tubules, which in turn enter the ductile efferent's. They link the rete testis and the mesonephric or Wölffian duct, which becomes the ductus deferens [10].

✓ **Descent of the Testes**

Testicular descent occurs in two phases: transabdominal descent and inguinoscrotal migration. Initial transabdominal descent occurs in the first trimester of gestation. At approximately 22-25 weeks of gestational age, the testes are located at the internal ring. The inguinoscrotal phase of testicular descent, which is androgen dependent, occurs between 25-30 weeks. Given the relatively late migration of testes through the inguinal canal into the scrotum, the prevalence of cryptorchidism is higher in premature boys in the first months of life (1-3% in full-term and 15-30% in premature male infants). Descent of the testes in the scrotum is probable in premature boys during the first months of life, but is unlikely after six months of corrected age. Obtaining the gestational age is so critical to the proper and timely referral of a child with persistent undescended testes to a surgical specialist [11]. Calcitonin gene-related peptide (CGRP) from genitofemoral nerve suggested to mediate the inguinoscrotal testicular descent [12]. During the descent of testis, the peritoneum of the abdominal cavity forms an evagination on each side of the midline into the anterior abdominal wall. This evagination, the processus vaginalis, follows the course of the gubernaculum-testis into the scrotal swellings. The processus vaginalis, accompanied by the muscular and fascial layers of the body wall, evaginates as the scrotal swelling, forming the inguinal canal [13].

GROSS ANATOMY

- ***The Testis:*** The adult testes are 4 to 5 cm long, 3 cm wide and 2.5 cm deep and have a volume of 30 ml. They are enclosed in a tough capsule comprising (1) The visceral tunica vaginalis (2) The tunica albuginea, with collagenous and smooth muscle elements and (3) The tunica vasculosa [14].
- ***The Epididymis:*** This is a convoluted duct that measures about 6 m when unravelled. It is intimately related to the testis, with its head lying on the upper pole, its body along the posterolateral aspect of the testis and its tail lying inferiorly. From here it turns back on itself at an acute angle to become the vas deferens. The efferent ductules of the testis drain sperm to the head of the epididymis. The epididymis concentrates, stores and transports sperm to the ejaculatory ducts and has a role in its maturation [14].
- ***The Vas deferens:*** This extends from the tail of the epididymis through the scrotum, inguinal canal and pelvis to fuse with the duct of the seminal vesicle to form the ejaculatory duct in the prostate gland. The vas deferens and epididymis are supplied by branches of the inferior vesical artery (deferential artery) and inferior epigastric artery (cremasteric artery) [14].
- ***The Spermatic cord :*** The spermatic cord contains the vas deferens, along with all of the arterial supply, draining veins, lymphatics and nerves of the testes. It is tightly covered by a fibrous sheath comprised of internal spermatic, cremasteric and external spermatic fascial layers derived from transversalis, internal and external oblique abdominal fasciae as it passes through the anterior abdominall wall [15].
- ***The Scrotum***

The scrotal skin is pigmented, hair bearing, devoid of fat, and rich in sebaceous and sweat glands. A midline raphe runs from the urethral meatus to the anus and represents the line of fusion of the genital tubercles. Deep to this raphe, the scrotum is separated into two compartments by a septum [14].

The dartos layer of smooth muscle is continuous with Scarpa's, Colle's, and the dartos fascia of the penis. The testes are suspended by their cords in the scrotal compartments. As the testes descend, they acquire coverings from the layers of the abdominal wall, known as the *spermatic fascia*, that form part of the scrotal wall [14].

The anterior wall of the scrotum is supplied by the external pudendal vessels and the ilioinguinal and genitofemoral nerves [14]. The anterior vessels and nerves typically run parallel to the rugae and do not cross the raphe. The back of the scrotum is supplied by the posterior scrotal branches of the perineal vessels and nerves. In addition, the posterior femoral cutaneous nerve (S3) gives a perineal branch to supply the scrotum and perineum. In accordance with their origin, the spermatic fasciae have a blood supply (cremasteric, vasal, testicular) separate from that of the scrotal wall [14].

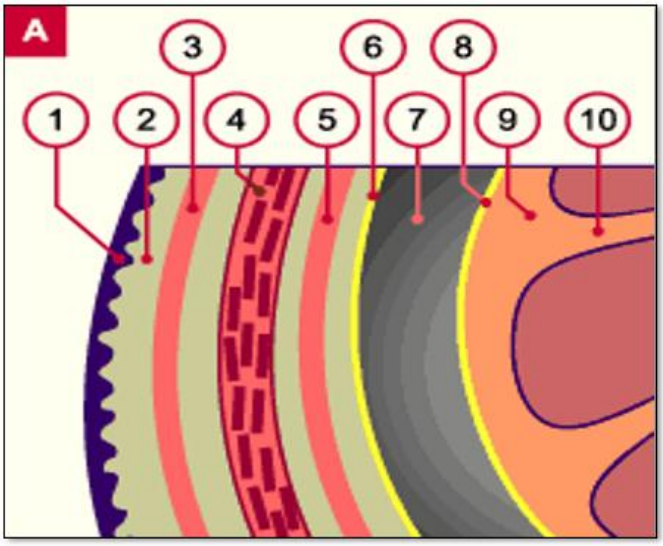

Fig. (1): Detail of the various layers that have formed in the scrotum by the end of the pregnancy ***(Quoted from human embryology organogenesis 2016).***

1-Epidermis
2-Dermis (tunica dartos)
3-External spermatic fascia
4-Musculuscremaster
5-Internal spermatic fascia
6-Parietal lamina of the tunica vaginalis
7-Virtual cavity between the twolayers of the tunica vaginalis
8-Visceral lamina of the tunica vaginalis
9-Tunica albuginea
10-Interlobular septum of the testis

THE BLOOD–TESTIS BARRIER

Large molecules cannot pass from the blood into the lumen of a seminiferous tubule due to the presence of tight junctions between adjacent Sertoli cells. The spermatogonia are in the basal compartment (deep to the level of the tight junctions) and the more mature forms such as primary and secondary spermatocytes and spermatids are in the adluminal compartment [16].

The function of the blood–testis barrier may be to prevent an auto-immune reaction. Mature sperm (and their antigens) arise long after immune tolerance is established in infancy. Therefore, since sperm are antigenically different from self tissue, a male animal can react immunologically to his own sperm. In fact, he is capable of making antibodies against them. Injection of sperm antigens causes inflammation of the testis (auto-immune orchitis) and reduced fertility. Thus, the blood–testis barrier may reduce the likelihood that sperm proteins will induce an immune response, reducing fertility and so progeny [16].

Temperature regulation

The testes work best at temperatures slightly less than core body temperature. The spermatogenesis is less efficient at lower and higher temperatures. This is presumably why the testes are located outside the body. There are a number of mechanisms to maintain the testes at the optimum temperature. Successful spermatogenesis is achieved at temperatures a few degrees below core body temperature. The **extra-abdominal location of the testes** is critical to spermatogenesis. The testes may be several Celsius degrees cooler than core body temperature [17].

In humans, failure of the testes to descend into the scrotum results in a condition referred to as cryptorchidism. Males with bilateral cryptorchidism are unable to produce sperm, but may well produce androgens at normal levels, and will generally have a normal masculinizing puberty [17].

The cremaster muscle is involuntary. These muscles work to contract the scrotum and to draw the testes towards the abdominal cavity when the testes are cold. They relax when the testes are too warm. Blood entering the scrotum from the abdomen through the testicular artery is warmer than blood

leaving the testes through the testicular vein. **Countercurrent heat exchange,** from blood in the testicular artery to blood in the plexus formed by the testicular veins, decreases the temperature of blood entering the testes [17].

Pathology of Cryptorchidism

Cryptorchidism means the absence of one or both testes from the scrotum and is generally synonymous with undescended testis (described as an empty scrotum) [18].

INCIDENCE AND CLASSIFICATION OF UNDESCENDED TESTES (UDT)

True UDT refers to any testis in which its migration arrests along the normal pathway of descent leading to its absence in the ipsilateral scrotum. While Cryptorchidism is failure of the testis to descend into the scrotum including all abnormalities of testicular descent as true undescended, ectopic, gliding, retractile and ascending testes [19].

A- Incidence: Undescended testis is present in about 1- 4.5% of newborns with a higher incidence in preterms (30-45%) and weighing less than 2500g (Ashley *et al.*, 2010. In infants born with undescended testes, the testes may descend into the scrotum in 75% of full-term neonates and in 90% of premature newborn boys in infancy and the incidence decreases to 0.8 - 1.2% at 1 year of age [19].

B - Classification of True UDT: classified according to the following :

a) Intra abdominal: The intra-abdominal testis is usually located just inside the internal ring, commonly within a few centimeters, although intra-abdominal testes have been observed anywhere along a line between the lower pole of the kidney and the internal ring. Testes may also lie at a high annular position at the internal ring. These testes have been referred to as "peeping," because they can move between the abdominal cavity and inguinal canal. Rarely, a testis is found in ectopic intra-abdominal positions such as in the perihepatic and perisplenic regions [19].

b) Intra canalicular (inside inguinal canal): The intracanalicular testis is occasionally difficult to palpate and by definition lies within the inguinal canal, between the internal and the external rings [19].

c) Prescrotal: It refers to the testis that lies just outside the external inguinal ring. It may be supra pubic or infra pubic. The emergent or suprapubic testis lies just beyond the external ring, above the level of pubic symphysis, and the infrapubic testis lies just below the pubic symphysis, often just outside the anatomy of scrotum in the retroscrotal space [19].

Other causes of absence of testes in the scrotum

1-Ectopic testis

Describes testes that after their descent and exiting the external inguinal ring do not follow the normal pathway into the scrotum. The most common site of ectopia is the superficial inguinal pouch between the external oblique aponeurosis and the subcutaneous tissue. Perineal, prepenile, transverse scrotal, femoral, and abdominal positions are other less common sites of ectopia. Ectopic testes are mechanically fixed in place, therefore requiring operative treatment. The cryptorchid testes have abnormal histology while ectopic testes have a normal histology. The most diagnostic difference clinically between ectopic and UDT is the shape of scrotum [19].

2 -Retractile testis: It is a descended testis that is withdrawn out of the scrotum by an exaggerated cremasteric reflex which is initiated by stroking the skin of the inner aspect of the thigh. The testis may retract out of the scrotum in the cold, on examination, on excitement or on physical activity. They most commonly present clinically between the ages of 3 and 7 years of age. Retractile testis does not require therapy. The retractile testis is truly not cryptorchoid, although there is a 32% risk of ascent when boys previously documented to have normally descended testes are found later in childhood to be cryptorchid [19].

3 -Gliding testis: These are testes that after their descent lie in a supra scrotal position, which can be manipulated into the scrotum by physical milking, but they differ from retractile testes in that they immediately return to their supra scrotal position after release of the manual tension. These testes have the same histology as the cryptorchoid testes arrested in the their true line of descent. The gliding testis is not a retractile testis but rather one that upon being manipulated to the upper portion of the scrotum immediately retracts [19].

4 -Anorchia (Vanishing testes - Empty scrotum): These testes are thought to be lost due to an antenatal or neonatal vascular accident (vanishing testis syndrome). Finding blind-ending gonadal vessels and a vas deferens either laporoscopically or at a retro peritoneal exploration is the hallmark of testicular absence [19].

If the testes are lost between 8 and 10 weeks, the baby will be born with ambiguous genitalia. This means that elements of both male and female internal

and external genitalia will be seen. Investigations for intersex disorder are needed in this case [20].

However, if the testes are lost after the critical phase of male differentiation between 12 and 14 weeks, the baby will have normal male internal and external genitalia (penis and scrotum), but the testes will be absent. This is known as congenital anorchia [20]. Congenital anorchia has been said to occur in 1 in 20.000 male and 1/177 in case of cryptorchidism [22].

DIAGNOSIS is done through Laboratory studies (Chromosomal analysis for karyotype, Endocrine screening for Testosterone, DHT, DHEA, ACTH and aldosterone, Electrolytes, urea and creatinine. Androgen receptor levels and 5alpha reductase levels, **Imaging: (**Pelvic and renal ultrasound. Adrenal glands may be seen to be enlarge, Genitography,CT and MRI scanning can help identify anatomy), and **Other procedures** include laparotomy or laparoscopy with or without gonadal biopsy. This can differentiate ovaries, testes and streak gonads [20].

5 -Testicular reascent: It is a very rare condition which occurs more commonly on the left side. A previously normal or a retractile testis can become high with a shortened spermatic cord that prevents the testis from staying in the scrotum (the ascending testis syndrome). It is usually diagnosed in those aged 8-10 years. Some sources say that this needs corrective treatment but others suggest a 'wait-and-see' approach for spontaneous descent until puberty [19].

ETIOLOGICAL AND RISK FACTORS FOR UDT

A- Epidemiological

Low birth weight (<2.5 kg), being small for gestation and prematurity is a risk [21].

Important factors common to all reports include pre-eclampsia, diabetes, obesity in the mother, in vitro fertilization and use of cosmetics by the mother have also been recognized as risk factors for development of cryptorchidism. This again implicates factors that may disrupt uteroplacental function, affecting fetal viability and development. Also breech presentation of the fetus, delivery by cesarean section or complicated delivery and a family history of cryptorchidism are risk factors [21]. Simultaneous presence of hypospadius and cryptorchidism has been shown to occur more commonly than would be predicted. Inheritance where the risk of undescended testes is 10.1 fold higher in male twins if present in one of them, 3.5 fold higher in males with a brother with undescended testes, and 2.3 fold higher in males with a father with the condition [23].

Cryptorchidism occurs at a much higher rate in a large number of congenital malformation syndromes. Among the more common are Down syndrome, Prader-Willi syndrome, Noonan syndrome. Kallmann's syndrome, Laurence-Moon-Biedl syndrome, Intersexuality/congenital adrenal hyperplasia, Prune belly syndrome. Mathers *et al.* [24].had investigated the possible relationship between cryptorcidism and prenatal exposure to a chemical called phthalate (DEHP) which is used in the manufacture of plastics. He found a significant association between higher levels of DEHP metabolites in the pregnant mothers and several sex-related changes, including incomplete descent of the testes in their sons .

B- Hormonal

Plasma FSH levels are often elevated in patients with testicular pathology, including patients with cryptorchidism. FSH stimulates Sertoli cells and therefore has an important role in spermatogenesis. Plasma FSH levels usually correlate inversely with spermatogenesis, and therefore FSH is considered the most clinically useful endocrine marker in the evaluation of infertile men. However, in children, circulating FSH, LH, and testosterone levels may not accurately reflect testicular development or the presence of testicular pathology [19].

Congenital undescended testes is often associated with hypogonadotropic- hypogonadism, decreased Leydig cell function, and inadequate androgenic effect due to diseases such as androgen receptor defect.

In utero testosterone deficiency can be caused by decreased LH, by impaired function of GnRH or LH receptors, or by loss of function mutations in the proteins involved in testosterone biosynthesis [19].

Müllerian Inhibiting Substance (MIS) is secreted by the fetal Sertoli cells and is responsible for regression of the müllerian ducts. MIS has also been implicated in effecting testicular descent [19].

Conflicting views on the role of androgen stimulation and gubernacular development resulted in the concept of an androgen-independent factor, descendin, a gubernacular specific growth factor. Normal gubernacular development was observed to occur in the presence of complete testicular feminization [19].

C- Gubernaculum

The gubernaculum appears at the seventh week of embryologic development.Once the testis has passed

through the inguinal canal and descent is complete, the bulb of the gubernaculum is resorbed. Clinical and experimental data indicate that hormones, transcription factors, and possibly neural factors influence development [19].

D- Epididymis:

The theoretical association uniting normal testicular descent to epididymal function is based on the observation that epididymal abnormalities often accompany cryptorchidism. The difficulty arises in that it is unknown whether epididymal anomalies are the cause or the result of the UDT. Epididymal abnormalities range from minor structural findings, such as elongation, to more complex anatomic aberrations of fusion, to complete disjunction, to an absent structure altogether [19].

COMPLICATIONS OF UNDESCENDED TESTES

- **Testicular cancer**

Testicular cancer usually begins in the cells in the testicle that produce immature sperm. A total of 10% of testis malignancies are associated with undescended testes and The risk is greater for undescended testicles located in the abdomen than in the groin.The age range during which testis tumors most frequently develop in these cases is 20-40 years[23].The most common types of testicular cancer encountered are seminoma and embryonal carcinoma. A germ-cell tumor was reported to occur in 64% of such cases. The other testicle is also more likely to develop cancer, even if it descended properly [23].

- **Fertility problems**

Low sperm counts, poor sperm quality and decreased fertility are more likely to occur among men who have an undescended testicle. A decrease in cells in the testicle that produce sperm has been found as early as 1 year old. [25]. 10% of infertile males have a history of undescended testes. The infertility risk is six fold higher in patients with bilateral undescended testes compared to patients with unilateral undescended testis or with a healthy population. (Chung and Brock [26] emphasized the importance of early treatment after detecting that the rates of germ cell loss and Leydig cell loss were 2% and 1%, respectively, per month in untreated cases. Infertility rate increases with bilateral UDT more than with unilateral UDT.

Other complications related to the abnormal location of the undescended testicle include :

- **Testicular torsion :**

Testicular torsion is the twisting of the spermatic cord, which contains blood vessels, nerves and the tube that carries semen from the testicle to the penis (vas deferens) and if not treated promptly, it might result in the loss of the testicle. Testicular torsion occurs 10 times more often in undescended testicles than in normal testicles. The risk for torsion is higher in adult patients with undescended testes compared to overall population [27].

- **Trauma :**

If a testicle is located in the groin, it might be damaged from pressure against the pubic bone [27].

- **Inguinal hernia :**If the opening between the abdomen and the inguinal canal is too loose, a portion of the intestines can push into the groin. (Lao *et al.*, 2012).

IMAGING APPROACHES

1. Magnetic Resonance Imaging (MRI)

Conventional MRI is non-invasive, free from radiation and produces excellent multiplanar images even without a contrast agent. ***(Gatti and Ostlie, 2007), Shah and Shah, 2006*** showed the overall diagnostic agreement of MRI with laparoscopy in 52% of cases.

When injected into the body, gadolinium contrast medium makes certain tissues, abnormalities or disease processes more clearly visible on a magnetic resonance imaging (MRI) scans. Gadolinium based contrast medium is sometimes called an MRI contrast medium or agent [28].

MRI contrast agents (usually gadolinium based contrast medium) improve diagnostic accuracy in some conditions such as inflammation and infectious diseases of the brain, spine, soft tissues and bones by making it easier for the radiologist to see what and where the problem is. The nature and extent of some testicular cancers and benign tumours is best seen and assessed using gadolinium contrast medium [28]. Nowadays, MRI could stand alone and perform better in identifying and locating cryptorchid testicles even without IV Gadolinium contrast injection. Even though MRI is more expensive than either ultrasound or computed tomographic scan, it may be clinically preferable to ultrasound because it allows global, multiplanar depiction of the anatomy of the structures and can distinguish testicles from lymph nodes by using specific orientation and sequences in axial or coronal plane films [28].

Advantages and Limitations of MRI

MRI has better soft-tissue contrast and multiplanar capability; however, when the testis is higher in the abdomen, the presence of bowel loops lowers the sensitivity for detecting the cryptorchid testis, however, MRI has few disadvantages,

including long scanning time and motion artifacts during the examination, the need for sedation in case of young children, and a higher cost than for US [30] **,**In addition MRI is contraindicated if any patient has electrically, magnetically, or mechanically activated implant (eg. cardiac pace maker, insulin pump biostimulator, neurostimulator, cochlear implant and hearing aids), intracranial aneurysms clips (unless made of titanium), ferromagnetic surgical clips or staples, metallic foreign body in the eye and metal sharpnels or bullets. Also patients with claustrophobia cannot be able to use MRI modality, unless they are under sedation or anaesthesia.

2. Diffusion Weighted Imaging (DWI)

Diffusion-weighted MRI (DWI) of the abdomen and pelvis, which has been widely used for diagnostic purposes, entails a contrast mechanism for evaluating pathologic changes in solid abdominal and pelvic organs. DWI depicts abnormalities on the basis of tumor cellularity and vascularity [31]. With DWI technique, information is extracted on the diffusion of water molecules, which reflects the degree of cellularity of tissue. A different image is produced than with conventional MRI sequences. Use of DWI therefore facilitates characterization of tissue at the microscopic level in a mechanism different from T1 and T2 relaxation [29].

The degree of restriction of water diffusion in biologic tissue is inversely related to tissue cellularity and the integrity of cell membranes. The motion of water molecules is more restricted in tissues with the high cellularity associated with numerous intact cell membranes (e.g., tumor tissue) [31].

Concordantly, intraabdominal testes are considerably more cellular than the adjacent organs and tissues and can be detected easily on DW images owing to their increased signal intensity [31].

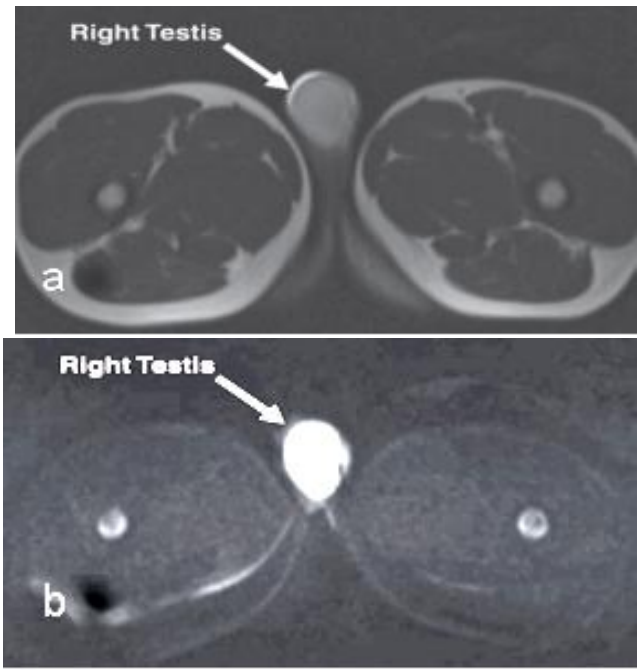

Fig. (2): 28-year-old man with normal descended right testis.

a, T2-weighted MR image shows normal descended right testis, which has equal to high signal intensity in comparison with normal parenchyma

b, Diffusion-weighted MR image with b value of 800 s/mm^2 shows marked hyperintensity of right testis [28].

Diffusion Imaging Principles

- **Brownian Motion:**

Molecular diffusion, or Brownian motion, was first formally described by Einstein in 1905. The term molecular diffusion refers to the motion that any type of molecule in a fluid (e.g. water) is randomly displaced as the molecule is agitated by thermal energy. In a glass of water, the motion of the water molecules is completely random and is limited only by the boundaries of the container. This erratic motion is best described in statistical terms by a displacement distribution. The displacement distribution describes the proportion of molecules that undergo displacement in a specific direction and to a specific distance (Figure 3) [32].

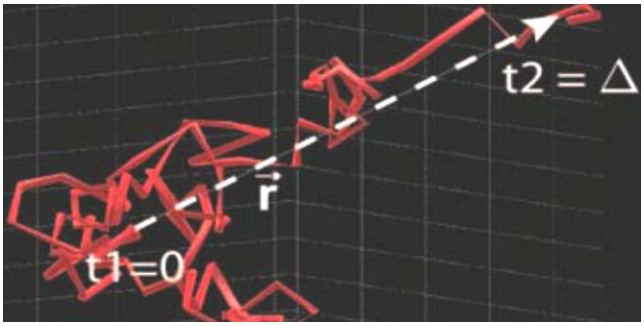

Fig. (3): Diagram shows the diffusion-driven random trajectory (red line) of a single water molecule during diffusion. The dotted white line (vector r) represents the molecular displacement during the diffusion [32].

Diffusion of Water Molecules in Tissues

DWI explores the random motion of water molecules in the body. Water molecules held in a container outside the body are in constant random brownian motion. This uninhibited motion of water molecules is free diffusion. By contrast, the movement of water molecules in biologic tissues is restricted because their motion is modified and limited by interactions with cell membranes and macromolecules [31].

There are two types of diffusion: Restricted diffusion for cellularity and intact cell membranes and Free diffusion for low cellularity and defective cell membranes [31]. The DWI signal is derived from the motion of water molecules in the extracellular space, the intracellular space, and the intravascular space [31].

Neverthless, water molecules in the intravascular space will have a greater diffusion distance because of blood flow than those in the extracellular and intracellular spaces. Clearly, the contribution of intravascular water diffusion to the measured DWI signal can vary among tissues. In tumors showing increased vascularity, the contribution of intravascular water diffusion to the MR signal may account for a significant proportion**.** The degree of restriction to water diffusion in biologic tissue is inversely correlated to the tissue cellularity and the integrity of cell membranes.

The motion of water molecules is more restricted in tissues with a high cellular density associated with numerous intact cell membranes (e.g., tumor tissue). The lipophilic cell membranes act as barriers to motion of water molecules in both the extracellular and intracellular spaces. By contrast, in areas of low cellularity or where the cellular membrane has been breached, the motion of water molecules is less restricted. A less cellular environment provides a larger extracellular space for diffusion of water molecules, and these molecules may also freely transgress defective cell membranes to move from the extracellular into the intracellular compartment [31].

Diffusion weighted imaging using spin-echo T2 weighted pulse sequence

Koh and Collins [31] described an MR experiment that could be applied to the detection and quantification of water diffusion in vivo. They adapted a standard T2-weighted spin-echo sequence by applying asymmetric pair of diffusion-sensitizing (bipolar) gradients around the 180° refocusing pulse. This approach is now the basis of many DWI sequences in clinical use today [31]. Static molecules acquire phase information from the first diffusion gradient, but information will be rephased by the second diffusion gradient without a significant change in the measured signal intensity. By comparison, moving water molecules acquire different phase information from the first gradient, but because of their motion, their signal will not be completely rephased by the second gradient, thus leading to a signal loss [31]. Hence, the motion of water molecules is detected as attenuation of the measured signal intensity at DWI. The degree of water motion has been found to be proportional to the degree of signal attenuation [31]. The sensitivity of the DWI sequence to water motion can be varied by changing the gradient amplitude, the duration of the applied gradient, and the time interval between the paired gradients. On clinical MR scanners, the diffusion sensitivity is easily varied by changing the parameter known as the "b value," which is proportional to these three factors. When the b value is changed, it is usually the gradient amplitude, rather than the duration or time intervals between gradients, that is altered [31].

Water molecules with a large degree of motion or a great diffusion distance (e.g., within the intravascular space) will show signal attenuation with small b values (e.g. b= 50–100 s/mm^2). By contrast, large b values (e.g., b= 1,000 s/mm^2) are usually required to perceive slow-moving water molecules or small diffusion distances because these show more gradual signal attenuation with increasing b values [31].

Disadvantages of T2 spin echo pulse sequence

Minor bulk patient motion was enough to obscure the much smaller molecular motion of diffusion could be determined by original spin-echo T2-weighted sequence, also the diffusion gradients were only

applied in one direction, so acquisition of multi-section, multidirectional images can take several hours with spin-echo methods [33].

Echoplanar Imaging (EPI)

With the development of high-performance gradients, DWI can be performed with an echo-planar spin-echo T2-weighted sequence. The substitution of an echo-planar spin-echo T2-weighted sequence markedly decreased imaging time and motion artifacts and increased sensitivity to signal changes due to molecular motion. As a result, the DW sequence became clinically feasible to perform [33].

In EPI, multiple lines of imaging data are acquired after a single radiofrequency (RF) pulse excitation. Like a conventional spin echo (SE) sequence, a SE EPI sequence begins with 90° and 180° RF pulses. However, after the 180° RF pulse, the frequency-encoding gradient oscillates rapidly from a positive to negative amplitude, forming a train of gradient echoes [33].

- ***Single-shot and Multi-Shot EPI***

EPI can be performed by using single or multiple excitation pulses ("shots"). The number of shots represents the number of TR periods required to complete the image acquisition. The number of shots is equal to the total number of phase-encoding steps divided by the echotrain length. For example, if the number of phase-encoding steps is 256 and the echo train length is eight, then the number of shots equals 256/8 or 32. In single-shot (snapshot) EPI, all of the data are acquired with only one shot. However, the image acquisition matrix is typically no larger than 128 x 128 [32]. Single-shot EPI is limited by lower resolutions (~128 x 128), image blurring, localized signal loss, and image distortions. Distortions and signal loss occur predominantly at boundaries between tissue and air, due to the local change of magnetic field strength. To achieve higher resolution and reduce the image distortion and signal loss, multishot EPI can be performed [32].

Limitations of DWI

On DW images, hyperintensity due to susceptibility artifacts around air-containing bowel were dismissed and not recorded as testes. On conventional MR images, elliptic areas hypointense on fat-suppressed T1-weighted images and hyperintense on T2-weighted images were recorded as testes in the aforementioned locations. On the combined DW and conventional MR images, conventional MRI was used for anatomic location of hyperintense elliptic areas on the DW images. On DW images, testes were recorded for focal areas of hyperintensity that did not represent T2 shine-through from fluid-containing structures [28].

3. Ultrasonography (USG)

Ultrasonography (USG) remains the most common investigation ordered by a physician in a child with non-palpable testis before referring him to a pediatric urologist or pediatric surgeon. **Advantages of USG include** lesser cost, non-invasive modality with no risk of radiation exposure and no need of anesthesia in young children. It is a real time and repeated examinations can be performed. **Limitations include** low sensitivity in identifying non-palpable abdominal testes preoperatively and operator dependent [4].

Ultrasound cannot differentiate between non-viable testes from surrounding inguinal tissue, and bowel gas often precludes localization of intraabdominal testes [5].

Abdominal-scrotal ultrasound is unnecessary in the preoperative evaluation of boys with non-palpable intraabdominal testis, because it would not change the surgical management of boys with this condition [5].

Elder [34] demonstrated that 61% of testes not identified by USG were palpable on physical examination. The study described three situations where USG has some role in cryptorchid patients: (1) In obese boys where an inguinal testis can be difficult to palpate and diagnostic laparoscopy has an increased complication rate; (2) In boys with non-palpable testis after previous orchiopexy to demonstrate whether the testis is viable and demonstrate its position; (3) In neonates with disorder of sexual differentiation to look for enlarged adrenals, to determine whether a uterus is present and to identify whether a gonad is a testis or an ovary. A recent meta-analysis by ***Tasian and Copp*** [4] demonstrated poor efficacy of USG in boys with non-palpable testes**.**

Kanemoto et al. [30] had the sensitivity, specifity and accuracy of USG in the diagnosis of non-palpable testes was 76-88%, 100% and 84-91% respectively. However, ***Shah and Shah*** [2] have shown the overall diagnostic agreement of USG with laparoscopy in only 19% of cases**.**

Appearance of Normal Testes in Ultrasound

The testes may be imaged by ultrasound as oval structures having a homogeneous granular echotexture with uniform medium-level echoes. The mediastinum may be identified as a linear echogenic band running superolaterally. Occasionally the rete

testis is prominent as multiple anechoic structures in the posterosuperior aspect of the testis. The septae may sometimes be appreciated linear echogenic thin bands running through the testis. These can be more readily appreciated if the testis is swollen in pathological conditions. On longitudinal scans, the upper and lower poles are identified [15].

Vessels are often identified running through the testis and hypoechoic linear structures. The appendix of the testis may be identified on high resolution images, especially if outlined by fluid. The head of the epididymis is seen to rest on the upper pole posteriorly. The body of the epididymis is seen posterolateral to the testis, and the spermatic cord is medial to the epididymis. The various parts of the epididymis are better seen if outlined by fluid [35].

The scrotal septum is seen between the testes. A small amount of anechoic fluid may surround the normal testis. The appendix of the epididymis may be seen if fluid is present [15]. The tortuous veins of the pampiniform plexus may be seen related to the cord above the upper pole. Slow venous flow may be demonstrated by colour Doppler techniques [15].

Rarely, an undescended testis can be confused with an inguinal hernia; real time peristalsis confirms the presence of bowel. Persistence of pars infravaginalis gubernaculi has been mistaken for the testis. The presence of an echogenic band (mediastinum testis) identifies the maldescended testis [35].

4. *Computed Tomography (CT)*

Appearance of Testes in CT

Cryptorchid testis is seen as an oval soft-tissue mass along the expected course of testicular descent. Uniform enhancement is seen with intravenous (IV) radiographic contrast [36].

CT is almost as accurate as US in detecting an undescended testis in the inguinal region. CT is much better than US in detecting an undescended testis that is located abdominally. In one study evaluation of undescended testis, CT scan and ultrasonographic accuracy were 96% and 91%, respectively.

Occasionally, bowel loops and lymph nodes can mimic the undescended testis. CT scanning is much better at differentiating the undescended testis from the bowel loop. A lymph node can be differentiated readily by the presence of fatty hilum and its characteristic location [36]. However, CT is infrequently used in boys with non-palpable testes as it is unreliable and carries the risk of radiation [36].

5. *Testicular Venography*

Testicular venography has fallen out of favor because of the availability of noninvasive tests. The following findings are diagnostic; demonstrated the presence of the pampiniform plexus, visualization of testicular parenchyma, **a blind-ending** testicular vein (usually indicates **absent** testis). It is accurate but invasive technique. Thus, it is not preferred [35].

6. *MR Venography (MRV)*

Gadolinium infusion MR venography is an alternative, non-invasive method of evaluating the undescended testis, especially the vanishing testis [37].

In the study done by ***Lam et al.*** [37] on 34 patients presenting with 44 impalpable testes. They detected twenty-six hypoplastic canalicular testes, two testes at pelvic skinfold, four atrophic testes in the scrotum, and five intraabdominal testes were detected on both routine MR imaging and MR venography. Five “vanishing” testes in the scrotum and two at the groin region were detected by MR venography but not on MR imaging. The location of the testis was determined on T2 weighted images, as small hyper intense focus, whereas on MR venograms, the location of the testis was determined by the detection of a bright linear enhanced pampiniform venous plexus. The testis was described as hypoplastic if its size was similar or slightly smaller than the normal one. Vanishing testis was diagnosed if the bright linear enhanced pampiniform venous plexus, identified on the MR venography, but the testis could not be identified on T1- and T2-weighted sequences. If both MR venography and T1- and T2-weighted MR imaging failed to identify the testis and the pampiniform venous plexus, the testis was considered unidentified [37]. The imaging findings were correlated with surgical exploration or laparoscopic findings. The accuracy ranges from 88% to 100%, depending on the expertise of the surgeons. The surgeons were aware of the imaging findings, and the surgical approach was planned according to the MR imaging and MR venography findings. MR venography is clearly better than MR imaging or sonography in identifying the testis [37].

RADIOLOGICAL APPEARANCE OF UNDESCENDED TESTES BY MRI AND DWI

Magnetic Resonance Imaging (MRI)

MRI is the best cross-sectional modality to assess crypto-orchidism (replacing CT scan). It has a higher sensitivity than ultrasound (~90%) and a higher specificity (100%).

The tunica albuginea, mediastinum testis and fibrous septae are of low signal intensity compared with the high signal intensity of normal testicular

tissue on T2-weighted imaging such as the appearance of the corpus cavernosum penis. The testis is of homogeneous low to intermediate signal intensity on T1-weighted imaging and the epididymis is of variable intensity [29].

Diffusion Weighted Imaging (DWI)

Diffusion-weighted MRI (DWI) a non-invasive method has been established as a useful functional diagnostic tool in urogenital imaging. With DWI technique, information is extracted on the diffusion of water molecules, which reflects the degree of cellularity of tissue. A different image is produced than with conventional MRI sequences. Use of DWI therefore facilitates characterization of tissue at the microscopic level in a mechanism different from T1 and T2 relaxation [29].DWI is used to visualize changes in the translational (Brownian) motion of water molecules, and can provide tissue contrast, thus differing from conventional MRI. In the testes, edematous tissue rich in intracellular water or highly cellular tissue composed of Sertoli and Leydig cells can show altered patterns of water diffusion [31]. The degree of restriction of water diffusion in biologic tissue is inversely related to tissue cellularity and the integrity of cell membranes. The motion of water molecules is more restricted in tissues with the high cellularity [31].

Atrophic testes show low signal intensity on the T2 – weighted images, the signal intensity of the testes was low because of its smaller size and remarkable atrophy in the seminiferous tubules, on diffusion, however, the signal intensity was low owing to the hypocellularity of the atrophic testes, so it can be speculated that testes with low signal intensity on DW are no longer viable [29]**,** Fat-suppressed T2- weighted imaging was considered suitable for distinguishing between the testes and lymph nodes, as the lymph node has lower signal intensity than the testes[29]. Non-malignant lymph nodes have homogeneous high signal intensity on images obtained at a b value of 0 s/mm^2, whereas they have low signal intensity at a b value of 1,000 s/mm^2.

Diffusion-weighted MRI (DWI) of the abdomen and pelvis, which has been widely used for diagnostic purposes, entails a contrast mechanism for evaluating pathologic changes in solid abdominal and pelvic organs. On images with low b value, fluid-containing structures such as the bowel contents, urinary bladder, and gallbladder have high signal intensity, and the testes have mild to low signal intensity. On images with a high b value of 800-1000 s/mm^2, the bowel contents are suppressed, and the testes have high signal intensity, therefore, we can easily visualize undescended testes using DWI with a high b value [29].

CONCLUSION

Diagnostic imaging has been utilized to determine the anatomic location of non-palpable testes. Accurate pre-surgical localization of the testis could spare a child an operation in the setting of an absent testis or limit the extent of surgery if the testis can be definitively identified.

Since MRI is noninvasive imaging tool, does not involve ionizing radiation and yields multiplanar images but it is sometimes less efficient in locating intra-abdominal functioning testicles and it fails to locate most of the atrophied testicles. Additional MRI assessments, as fat-suppressed T2WI and DWI are useful methods to improve the accuracy and sensitivity of diagnosis of non-palpable testes.

MRI is a noninvasive technique, without the use of ionizing radiation, it can be used for localization of non-palpable UDT, especially compared to ultrasonography, which has little clinical benefit.

Based on our findings, we suggest that a combination of DWI and conventional MRI including Fat-supp. T2WI sequence is the most accurate means of detecting and localizing non-palpable undescended testes. The findings of DWI complement the information on the location of undescended testes obtained with conventional MRI. In addition, DWI is helpful in detection of testicular viability or atrophy properly before the operation.

REFERENCES

1. **Abd-ElGawad EA, Abdel-Gawad EA, Magdi M, Al-Minshawy SM (2015):** Magnetic resonance imaging for detection of non palpable undescended testes: Diagnostic accuracy of diffusion-weighted MRI in comparison with laparoscopic findings. The Egyptian Journal of Radiology and Nuclear Medicine, 46(1):205-10.
2. **Amar Shah and Anirudh Shah (2006):** Impalpable Testes–Is Imaging Really Helpful? Indian Pediatrics, 43:720-723.
3. **Miller DL, Kwon D, Bonavia GH (2009):** Reference levels for patient radiation doses in interventional radiology: proposed initial values for US practice. Radiology., 253(3):753-64.
4. **Tasian GE, Copp HL (2011):** Diagnostic performance of ultrasound in nonpalpable cryptorchidism: a systematic review and meta-analysis. Pediatrics, 127(1):119-28.

5. Krishnaswami S, Fonnesbeck C, Penson D, McPheeters ML. Magnetic resonance imaging for locating nonpalpable undescended testicles: a meta-analysis. Pediatrics,131(6):e1908-16.
6. **Muhi A, Ichikawa T, Motosugi U, Sou H, Nakajima H, Sano K, Sano M, Kato S, Kitamura T, Fatima Z, Fukushima K (2001):** Diagnosis of colorectal hepatic metastases: Comparison of contrast-enhanced CT, contrast-enhanced US, superparamagnetic iron oxide-enhanced MRI, and gadoxetic acid-enhanced MRI. Journal of Magnetic Resonance Imaging , 34(2):326-35.
7. **Qayyum A (2009):** Diffusion-weighted imaging in the abdomen and pelvis: concepts and applications. Radiographics, 29(6):1797-810.
8. **Bozkurt M, Doganay S, Kantarci M, Yalcin A, Eren S, Atamanalp SS, Yuce I, Yildirgan MI (2011):** Comparison of peritoneal tumor imaging using conventional MR imaging and diffusion-weighted MR imaging with different b values. European journal of radiology, 80(2):224-8.
9. **Kučinskas L, Just W (2005):** Human male sex determination and sexual differentiation: pathways, molecular interactions and genetic disorders. Medicina, 41(8):633-40.
10. **Lewis JM, Kaplan WE, Caroppo E, Zirkin BR, Papadopoulos V, Hardy MP, Alukal JP, Lamb DJ, Niederberger CS, Makhlouf AA, Turner TT (2009):** Anatomy and embryology of the male reproductive tract and gonadal development. Infertility in the Male. 4th ed. New York.
11. **Kavoussi LR, Wein AJ, Novick AC *et al.* (2007):** Campbell-Walsh Urology, 9th edn, vol. IV, chapter 127. Philadelphia: Saunders company, Pp:3761-98
12. **Niikura H, Okamoto S, Nagase S, Takano T, Murakami G, Tatsumi H, Yaegashi N (2008):** Fetal development of the human gubernaculum with special reference to the fasciae and muscles around it. Clin Anat., 21(6);547-57.
13. **Gordon G and Gallup J (2009):** On the Origin of Descended Scrotal Testicles: The Activation Hypothesis. Evolutionary psychology, 7(4): 517-526.
14. **James D (2007):** Brooks: Anatomy of the lower urinary tract and male genitalia. In: Louis R. Kavoussi, Andrew C. Novick, Alan W. Partin, Craig A. Peters, eds. Campbell – Walsh Urology, 9th ed. Philadelphia: Saunders, 2:77.
15. **Ryan S, McNicholas M, Eustace S (2011):** Anatomy for diagnostic imaging (3rd edition) Elsevier limited, 6:236-239
16. **Linlin Su, Dolores DM, Cheng CY (2011):** Drug transporters, the blood-testis barrier, and spermatogenesis. J. Endocrinol., 208(3):207-23.
17. **Currie D (2009):** The Regulation of testicular temperature (available from http://faculty. etsu.edu/currie/ temperature.htm).
18. **Williams EV, Appanna T, Foster ME (2001):** Management of the impalpable testis: A six year review together with a national experience. Postgrad Med J., 77:320–2.
19. **Francis X Schneck and Mark F (2007):** Bellinger: Abnormalities of the testes and scrotum and their surgical management. In: Louis R. Kavoussi, Andrew C. Novick, Alan W. Partin, Craig A. Peters, eds. Campbell- Walsh Urology, 8(3):2353-93.
20. **Lambert SM, Vilain EJ, Kolon TF (2010):** A practical approach to ambiguous genitalia in the newborn period. Urol Clin North Am., 37(2):195-205.
21. **Marijn M. Brouwers *et al.* (2012):** Risk factors for undescended testis. Journal of Pediatric Urology, 8(1): 59-66
22. **Aynsley-Green A, Zachmann M, Illig R, Rampini S, Prader A (1976):** Congenital bilateral anorchia in childhood : a clinical, endocrine and therapeutic evaluation of twenty one cases. Clin Endocrinol (Oxf.), 5:381-391
23. **Hutson JM, Balic A, Nation T, Southwell B (2010):** Cryptorchidism. Semin Pediatr Surg. ,19:215–224.
24. **Mathers MJ., Sperling H., Rübben H., Roth S (2009):** The undescended testis: diagnosis, treatment and long-term consequences. Dtsch Arztebl Int., 106:527-532.
25. **Kliegman RM *et al.* (2011):** Nelson Textbook of Pediatrics. 19th ed. Philadelphia, Pa.: Saunders Elsevier, 539:1858-1863.
26. **Chung E and Brock GB (2011):** Cryptorchidism and its impact on male fertility: a state of art review of current literature. Can Urol Assoc J., 5:210–214.
27. **Walsh TJ, Dall'Era MA, Croughan MS, Carroll PR, Turek PJ (2007):** Prepubertal orchiopexy for cryptorchidism may be associated with lower risk of testicular cancer. J Urol. ,178:1440–1446.
28. **Kantarci M, Doganay S, Yalcin A, Aksoy Y, Yilmaz-Cankaya B, Salman B (2010):** Diagnostic performance of diffusion-weighted MRI in the detection of non-palpable undescended testes: Comparison with conventional MRI and surgical findings. AJR Am J Roentgenol. ,195:268–73.
29. **Kato T, Kojima Y, Kamisawa H, Takeuchi M, Mizuno K, Sasaki S, Kohri K, Hayashi Y (2011):** Findings of fat-suppressed T2-weighted and diffusion-weighted magnetic resonance imaging in the diagnosis of non-palpable testes. BJU international, 107(2):290-4.
30. **Kanemoto K, Hayashi Y, Kojima Y, Maruyama T, Ito M, Kohri K (2005):** Accuracy of ultrasonography and magnetic resonance imaging in the diagnosis of non-palpable testis. Int J Urol., 12:668–72.
31. **Koh DM, Collins DJ (2007):** Diffusion-weighted MRI in the body: applications and challenges in oncology. AJR., 188:1622–1635
32. **Patric A, Fonasson L, Philipp M *et al.* (2006):** Understanding diffusion MR imaging techniques: From scalar diffusion-weighted Radiographics imaging to diffusion tensor imaging and Beyond Radiographics , 26: 221.
33. **Amin MP, Mirowitz SA, Brown JJ *et al.* (2001):**Principles and applications of echo-planar imaging. A review for the general radiologist. Radiographics , 21: 767-779.
34. **Elder JS (2002):** Ultrasonography is unnecessary in evaluating boys with a non-palpable testis. Pediatrics, 110:748–51.
35. **Dogra VS, Haddad JL, Coombs BD (2013):** Cryptorchidism Imaging. (available from http://emedicine. medscape.com/article/377971).
36. **Bertolotto M and Trombetta C (2012):** Scrotal pathology 1st ed. Springer Berlin Heidelberg, 27: 301-312
37. **Lam WW, Tam PK, Ai VH, Chan KL, Chan FL, Leong L (2001):** Using gadolinium-infusion MR venography to show the impalpable testis in pediatric patients. American Journal of Roentgenology,176(5):1221-6.