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**ADVANCEMENT IN TREATMENT TECHNOLOGY FOR UTERINE  
LEIOMYOMA**

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**ABSTRACT**

Uterine leiomyomass, or fibroids, represent a major public health problem. This is most common female pelvic tumor, typically reported to occur in 20–40% of reproductive aged women, and up to 70% of white and 80% of black women by the age of 50 years. Most fibroids are asymptomatic, but nearly half of women with fibroids have significant and often disabling symptoms including heavy menstrual bleeding, pain and pressure symptoms. Traditionally, symptomatic fibroids have been treated with myomectomy or hysterectomy performed by laparotomy. In an effort to reduce the cost, morbidity and lifestyle impact of major surgery, various less invasive or non-surgical procedures, new treatment approaches have become available to women with symptomatic fibroids. Undoubtedly the most significant therapeutic innovation has been the advent of uterine artery embolization (UAE) as a form of non-surgical management. New technology has provided additional minimally invasive options such as percutaneous laser ablation, cryoablation, transvaginal uterine artery occlusion and magnetic resonance imaging (MRI)-guided focused ultrasound that are currently under intense investigation. Furthermore, new medications have been introduced, that show promise for practical, long-term medical therapy for symptomatic fibroids.

**KeyWord:** Leiomyoma, Hysterectomy, Myotomy, Uterine artery embolisation, Laproscopic, Gonadotrophin releasing hormones.

**INTRODUCTION**

Smooth-muscle tumors of uterine origin encompass a broad family of neoplasms. The leiomyoma, by far the most common of all the neoplasms. It is a benign smooth-muscle tumor that most commonly affects the body of the uterus but may also be found in the cervix, broad ligament, and, rarely, the ovary. This form of tumor can also occur outside of the Mullerian tract, where pathologic criteria for diagnosis differ significantly<sup>[1]</sup>. The collagen content of the tumor gives it a hard, fibrous texture, thus the name fibroid.<sup>[2]</sup> They are typically asymptomatic but some patients' show symptoms.

Generally, Women presents two types of complaints-abnormal uterine bleeding and / or lower abdomen pressure related symptoms. Various terminologies are used to characterize this uterine tumour myofroma, Fibromyoma, leiomyofibroma, leiomyoma, fibroma, Myoma, and Fibroids. The designation “Fibroid” is least accurate. Nonetheless it is the most frequently used diagnostic term in both scientific and lay literature. Leiomyoma accurately describes this neoplasm and refers to any benign tumor of smooth-muscle origin.<sup>[3]</sup> They are multiple in up to 84% of women. Fibroids have been reported to occur in up to 70% of women by the age of 50 years and are especially common in black women, who also often have more severe disease. These benign tumors are hormone dependent, responding to both estrogen and progesterone. Early age at menarche and obesity are risk factors for the development of fibroids, likely due to the increased exposure to estrogen. The majority of women with fibroids are asymptomatic; however, 20-50% of them have symptoms such as menorrhagia, pelvic pain and Infertility, or complications during pregnancy. A large fibroid can present as an abdominal mass or with symptoms secondary to mass effect, e.g., constipation and urinary frequency or retention. Rarely, the patient may present with hydronephrosis or bowel obstruction<sup>[4]</sup>. The fact that fibroids occur during the reproductive years and regress after menopause indicates a growth dependent on ovarian hormones<sup>[5]</sup>. Increasingly more women with uterus leiomyomatus desire to have children at a later age. In addition, progressively more women with myoma conditional complaints who have finished their family planning wish to retain their uterus<sup>[6]</sup>. Surgical management of uterine fibroids has changed from laparotomy to minimally invasive surgery<sup>[7]</sup>. Treatment innovations have been slow, perhaps because many women have asymptomatic fibroids, myomas are benign and mortality is very low. If hysterectomy was the treatment options given; some women choose to bear with the symptoms and stop seeking treatment.<sup>[8]</sup> Regardless of their generally benign neoplastic character, Uterine fibroids are responsible for significant morbidity in a large segment of the female population. Recent technological advances have introduced newer, less invasive techniques that can remove part or most of the fibroids, but do not eliminate fibroid redevelopment or adhesion formation<sup>[9]</sup>.

### **Search Strategies**

We identified all English language medical papers published in the period 2000-2010 by means of the Pub Med electronic database using the following search terms, fibroid, Diagnosis of Fibroids, technology used for uterine fibroid, medical interventions, classification, Symptoms, USG. MRI, Hysterectomy, laparoscopic myomectomy, Cross-references picked up during the review search was also selected if they were not included initially. Both prospective and retrospective articles were considered. Studies presented at meetings or congresses, with only abstracts available, were not included

### **Signs and symptoms**

Abnormal uterine bleeding with longer, heavier menstrual periods. Bleeding between menstrual periods occurs in some women. Fatigue caused by anemia (low blood count) from excessive menstrual blood loss. Pelvic pressure when fibroid tumor growth causes an enlarged uterus. Urinary Frequency when the enlarged uterus presses on the bladder.

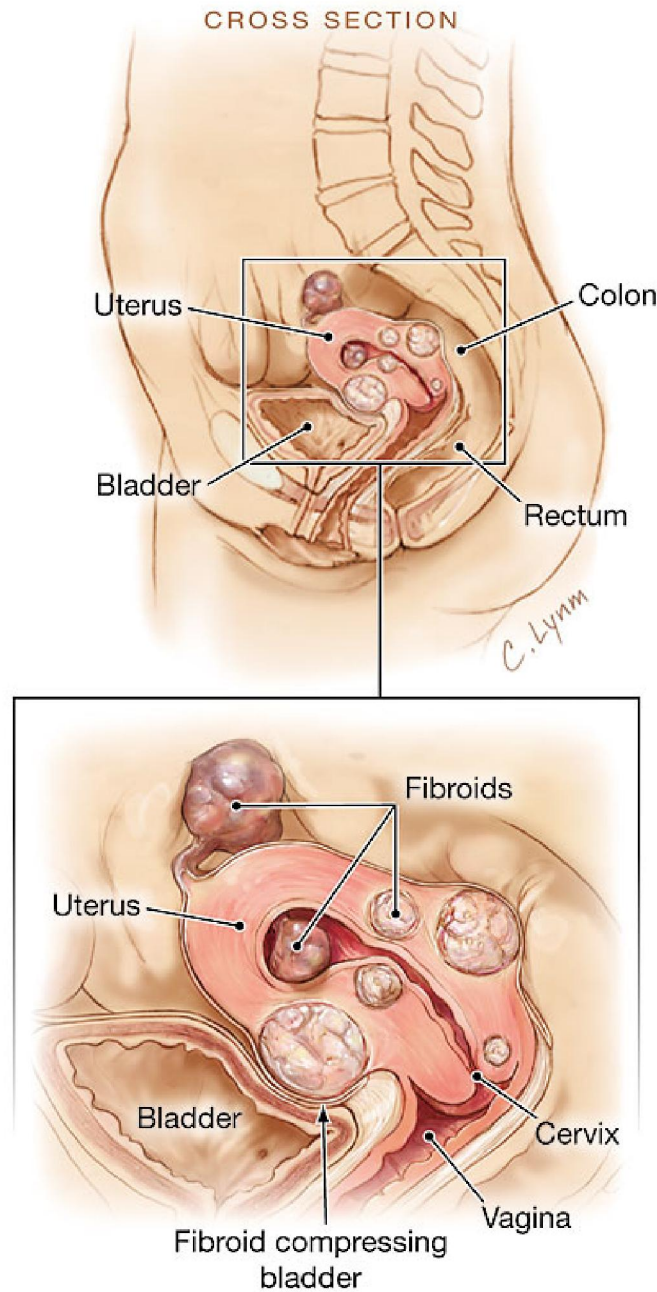
Infertility preventing pregnancy in some women; in others, miscarriage can occur. Pain in the pelvic region due to worsening menstrual cramps or pressure from the fibroids on other internal organs. Infertility preventing pregnancy in some women; in others, miscarriage can occur.

### **Associated regions for Symptoms**

Common symptoms of leiomyoma include menorrhagia, pelvic congestion and pain, pressure symptoms, or self-discovery of a mass in the abdomen. In general, the deeper the leiomyoma is situated (submucosal type), the more likely will menstrual symptoms occur while the superficial ones (subserosal type) of significant size may cause pressure symptoms.<sup>[2]</sup> Vaginal bleeding may lead to iron deficiency anemia.<sup>[10]</sup> The association of leiomyoma with heavy menstrual bleeding is thought to be due to an increase in eudiometrical surface area. Both submucosal and intramural leiomyomas have the potential to cause this. Other possible explanations include an increase in local prostaglandin's production and the preferential compression on the venous return from the endometrium. Pressure symptoms from leiomyoma may be expressed as urinary frequency or constipation depending on whether the subserosal leiomyoma arises from the anterior or posterior wall of the uterus. Symptoms may be more obvious premenstrual when the uterus is engorged. Occasionally acute urinary retention may occur due to

compression of the urethra by the leiomyomatous uterus. Acute pelvic pain may occur from degenerative change and rarely from torsion of a pedunculated leiomyoma. The accurate assessment of the number, size and location of leiomyomas is important in matching the patient's symptoms as well as in deciding on the appropriate treatment.

#### Individual with uterine fibroids



**Figure 1**

Individual with uterine fibroids

### **Histopathology of Leiomyoma**

Breakthrough in histopathology we had one Eudimetrical stromal tumor, one Desmoids, one Primary uterine malignancy thought to be Fibroid. Kemp son and co-workers for four decades evaluated whether the cells show smooth muscle or eudimetrical stromal differentiation. Architectural features, such as fascicular alignment of the tumor cells and the presence of thick walled vascularity, favor with a smooth muscle tumor. The vessels in endometrial stromal tumor are mainly thin-walled capillaries in arching pattern. In difficult cases, immunohistochemical staining with this Desmin, CD-10, and caldesmon may aid in determining whether the cells are of smooth muscles or endometrial stromal origin. In endometrial stromal tumors infiltration of myometrium or vessels indicates malignant behavior. In smooth muscle tumors, despite of infiltrating pattern the clinical course may be benign. Fibroids without any features of malignancy, such as coagulative necrosis, significant atypia or increased mitotic index (MI), yet they do metastasize. There can be nodes in lung, lymph nodes.<sup>[11]</sup>

### **Classification of Myoma**

Uterine smooth muscle tumors are classified according to their morphologic features that include architecture, growth pattern, cellular characteristics and constituents of the intercellular stroma. While terminologies used for the pathologic diagnosis of various subtypes may be eloquent and histologically accurate, some of these are confusing for the clinician and may also be open to interpretation by different pathologists: the labeling of atypical leiomyomas epitomizes this intricate system. Clinically, it is probably more useful to classify them as either tumors with or tumors without recurrent and/or metastatic potential. The term "atypical leiomyoma" has been used to label tumors that have a low risk of recurrence and is synonymous with benign tumors. The latter are known variously as leiomyoma with bizarre nuclei, symplastic leiomyoma, or pleomorphic leiomyoma. Variants of benign uterine smooth muscle tumors, such as mitotically active leiomyoma, cellular and highly cellular leiomyoma, epithelioid leiomyoma, and myxoid leiomyoma each have distinctive hallmarks that enable subclassification. Nevertheless, they may occasionally possess one or more unusual features that are cause for alarm. Tumors that have a dissecting growth pattern, with or without extrauterine extension, may mimic malignancy both grossly and

microscopically. Different types of fibroids may affect reproductive outcome to a different extent, with submucous, intramural and subserosal fibroids being (in decreasing order of importance) a cause of infertility and pregnancy wastage<sup>[13]</sup>.

### **Diagnosis**

Clinical assessment by bimanual digital examination remains the basis in detecting the condition. However the diagnosis may be missed if the leiomyomas are small and the woman is obese or is tensed up during the examination. Pelvic examination cannot detect submucosal leiomyoma Pelvic ultrasound, either transabdomina or trans-vaginal, is accurate in making the diagnosis. Subserosal leiomyomas big enough to be felt abdominally are better viewed with the trans abdominal approach while submucosal leiomyomas are better viewed trans-vaginally. Transvaginal Sonohysterography (involving intrauterine injection of saline during vaginal scanning) further enhances diagnostic accuracy in the latter. Diagnostic hysteroscopy, which can perform under local or no anesthesia, is a useful procedure in differentiating submucosal leiomyoma from endometrial polyp and can assess the suitability of hysteroscopic resection of the leiomyoma. MRI provides a better image in delineating the exact location and characteristic of the leiomyomas, but the additional information provided may not be necessary for clinical management except when focused ultrasound therapy is contemplated. However, it should be considered for women in whom the nature of the pelvic mass is uncertain after pelvic ultrasound. It can also help to differentiate leiomyoma from adenomyoma, especially when myomectomy is contemplated. There is insufficient evidence to recommend CT scanning in leiomyoma assessment. Discomforts caused by a myoma are an absolute indication for treatment.

### **Growth Factors Identified in Fibroids: Transforming growth factor:**

#### **Basic fibroblast growth factor (BFGF)**

Both TGF-3 and bFGF are over expressed in leiomyomas compared with matched myometrium, and both factors may contribute to the enhanced growth of miomas. Leiomyomas are characterized by large amounts of ECM (extra cellular matrix), and contain abundant amounts of bFGF. It may therefore serve as a reservoir for bFGF and impact endometrial vasculature through a paracrine or local endocrine effect.<sup>[14]</sup>

**Epidermal growth factor (EGF)**

EGF receptors in fibroids are more sensitive to regulation by the ovarian sex steroids than those in the myometrium. More importantly, because the reduction of EGF receptor levels correlates with shrinkage of the fibroids as a result of the GnRH-agonist.

**Platelet-derived growth factor**

More PDGF receptor sites per cell are seen in leiomyomas than in the myometrium, although the PDGF receptor binding affinity in the tumor cells is lower than that of the myometrium.

**Vascular endothelial growth factor**

VEGF stimulates angiogenesis, which is essential for actively growing tumors, and VEGF is the most potent agent known for increasing capillary permeability, which could enhance the growth of fibroids by increasing their nutrient supply. VEGF could also have an indirect effect by inducing the proliferation of endothelial cells, which themselves produce a number of growth factors. In addition, VEGF acts synergistically with fibroblast growth factor (FGF) and it can release the angiogenic factor bFGF from its storage on heparan sulfates of the extracellular matrix, with the resulting combination of the two-angiogenic mitogens having a synergistic effect on angiogenesis. Further, the resulting availability of bFGF permits the expression of its mitogenic effect upon the smooth muscle cell.

**What are Gonadotropin-releasing hormone (Gn-RH) analogues**

Gonadotropin-releasing hormone (Gn-RH) analogues are synthetic derivatives of the native hypothalamic peptide with alterations in their chemical structure that result in changes in biologic activity. Several Gn-RH agonists are available for clinical use, and all act through the same mechanism: first to stimulate and then to inhibit gonadotropin and gonadal steroid secretion by down regulating the pituitary Gn-RN receptors.<sup>[15]</sup> These substitutions at positions 6 and 10 in the amino acid structure result in analogs that are 40–200 times more potent than native LHRH. Although the initial response to these agents is an elevation of serum gonadotrophin levels and with it increased concentrations of sex steroids, continuous administration results in suppression of the pituitary–ovarian axis, with decreased gonadotropin and sex steroid levels. The mechanism of this suppression is thought to be related to down regulation of the pituitary LHRH receptors. The

hypoestrogenic state induced by these agents' results in reduction in size of the uterus itself as well as many of the fibroids in the majority of patients. A variety of theories have been proposed for the pathophysiologic mechanism leading to this shrinkage of fibroids, including a reduction in uterine arterial blood flow.<sup>[16]</sup>

### **Medicines used in Management of disease**

Gonadotrophin-releasing hormone analogues (GnRHa) have been the most widely used, and while they do cause fibroid regression, they can only be used in the short term, as temporizing measures in the per menopausal woman, or pre-operatively to reduce fibroid size, influence the type of surgery, restore hemoglobin levels and apparently reduce blood loss at operation. They are notorious for rebound growth of the fibroids upon cessation of therapy, and have major side effects. GnRH antagonists avoid the initial flare effect seen with GnRHa therapy, but otherwise do not appear to have any additional advantages over GnRHa. Selective estrogen receptor modulators, such as raloxifene, have been shown to induce fibroid regression effectively in post-, but not pre-, menopausal women; even in the former group, experience with these drugs is limited, and they are associated with significant side effects. Aromatase inhibitors only appear to be effective in postmenopausal women, have potentially significant long-term side effects, and experience with their use is also limited. There are suggestions that the levonorgestrel intra-uterine system can cause dramatic reduction in menstrual flow in women with fibroids, but to date there have been no RCTs of its use in these women, in whom rates of expulsion of the device appear to be high. The progesterone antagonists mifepristone and asoprisnil have shown significant promise and warrant further research, as they appear to show efficacy in inducing fibroid regression without major side-effects. However, they and the other hormonal therapies that alter estrogen and progesterone production or function significantly (danazol, gestrinone) are not compatible with reproduction. Therefore, the quest for the ideal medical therapy for fibroid disease continues, and increasing understanding of fibroid biology is ushering in non-hormonal therapies, although all are confined to laboratory experimentation at present. In the meantime, surgical and radiological approaches remain the mainstay effective therapies.<sup>[17]</sup>



### Chinese Herbal therapy

The effectiveness of the Chinese herbal treatments for small to medium size fibroids has been demonstrated by clinical trials conducted in China and Japan. American practitioners of Chinese medicine have frequently reported success in treating fibroids, at least to the extent of alleviating common symptoms and thus avoiding surgery for their patients. Uterine myomas up to the size of a goose egg can be successfully treated with herbs to reduce the size to a comfortable level and, in many cases, to eliminate them. Larger myomas are usually treated with surgery.

Curing egg-sized uterine myomas with Chinese herb formulas is possible, but a larger size proves difficult to cure. Only in one case that they know of was a patient with a fist-sized myoma cured after using Wenjing Tang (Tang-kuei and Evodia Combination) long term. The cure probably had something to do with the patient's menopause." Japanese doctors usually prescribe formulas with cinnamon twig, persica, and moutan for dispelling blood stasis in the lower abdomen. Examples are Guizhi Fuling Wan (Cinnamon and Hoelen Formula), Taohe Zhengqi Tang (Persica and Rhubarb Combination), and Zhechong Yin (Cinnamon and Persica Combination); rhubarb is included in treatments when constipation is presented. Use of Cinnamon and Hoelen formula as a decoction, modified with the addition of achyranthes, oyster shell, and salvia plus others according to syndrome; the decoctions would have about 80-120 grams of herbs. There were 100 patients treated with these formulas, and it was claimed that 46 cases had the mass eliminated, and 34 had it shrunk by at least half. Treatment time was 1-7 months. In another study, a pill of Cinnamon and Hoelen Formula plus turtle shell, oyster shell, artemisia, blue citrus, dipsacus, phellodendron, astragalus, and selaginella (often used as an anticancer herb) was used; the herbs were powdered and formed into pills with honey, about 6.6 grams of herbs per pill, one pill taken each time, three times daily. Of 60 patients treated, 43 were said to be cured and 11 markedly improved using from 1-9 months of treatment. In several additional clinical reports on fibroid treatment, three herbs in Guizhi Fuling Tang were retained: persica, red peony, and moutan, but the herbs that give the formula its name, cinnamon and hoelen, were replaced by others that vitalize blood and regulate qi, such as zedoaria and cyperus. In others, the Cinnamon and Hoelen Formula was retained intact, and herbs were added to address bleeding, anemia,

pain, or qi deficiency. In a Japanese study of the mechanism of action of Cinnamon and Hoelen Formula, it was mentioned that shrinkage of uterine myoma occurred in 62% of the 110 cases treated, and that the treatments alleviated excessive menstrual bleeding and resulting anemia as well as dysmenorrhea. There were no significant changes in plasma levels of several hormones, including LH, FSH, PRL, and estradiol, indicating that the mechanism of action did not involve reduction of hormone stimulus to fibroid growth. It was noted that small myomas with smooth surface generating elevated levels of CA-125 appeared to be most responsive to treatment; elevated CA-125 often indicates adenomyosis, a fibroid-like condition with small masses of the uterine wall<sup>[18]</sup>.

### **Hysteroscopic myomectomy**

The clinical effects of these tumors are related to their local mass effect, resulting in pressure upon adjacent organs, excessive uterine bleeding, or problems related to pregnancy, including infertility and repetitive pregnancy loss. As a consequence of these local pressure effects and bleeding, uterine fibroids rank as the major reason for Hysteroscopic myomectomy is an established surgical procedure for women with excessive uterine bleeding, infertility or repeated miscarriages and the risk for recurrence of myomas<sup>[19]</sup> and also for those whose symptoms have not resolved with medical treatment<sup>[20]</sup>.

In this Procedure viewing the uterine cavity via the cervix with the aid of a telescopic instrument<sup>[21]</sup>. Hysterectomy had improved pelvic pain scores. Furthermore, hysterectomy eliminates uterine bleeding and the risk for recurrence of myomas<sup>[22]</sup>.

### **Minimally invasive surgery (MIS)**

Minimally invasive surgery (MIS) such as natural orifice surgery is perceived as a relatively recent development partly because many MIS techniques utilize new technology and devices. However, a natural orifice/MIS approach for hysterectomy (vaginal hysterectomy, VH) has existed for over a century. VH is typically thought of in the realm of the urogynecologist as a component of reconstructive pelvic surgery for pelvic organ prolapse. However, current evidence supports the use of VH in women with other benign conditions such as uterine fibroids and abnormal bleeding. Despite the evidence and availability of several MIS options for hysterectomy, the majority of hysterectomies continue to be performed via laparotomy. VH is the least invasive

approach to hysterectomy, and its use should be encouraged as the preferred MIS option for women requiring uterine removal for benign conditions<sup>[23]</sup>.

### **Laparoscopic myomectomy**

Laparoscopic myomectomy is the destruction of fibroids via a laparoscope passed through a small incision in the abdomen and then through the wall of the uterus.

It is still the best treatment option for symptomatic women with uterine fibroids who wish to maintain their fertility<sup>7</sup> Open myomectomy should be the route of choice when there are large subserosal or intramural fibroids, multiple fibroids or entry into the uterine cavity is to be expected.<sup>[24]</sup> This is done when a fibroid of <15 cm in size, and no more than three fibroids with a size of 5 cm. laparoscopic myomectomy has the advantages of small incisions, short hospital stay, less postoperative pain, rapid recovery and good assessment of other abdominal organs. Due to the concern of decreased ovarian reserve, uterine artery embolization is not advisable for these women<sup>[7]</sup>. Laparoscopic myomectomy is a suitable alternative to MLPT in women with 1 to 3 myomas. However, preoperative careful evaluation of the size and sites of the myomas is necessary to avert conversion and prevent complications<sup>[25]</sup>.

### **UAE: Uterine artery Embolisation**

Transcatheter uterine artery embolization (UAE) has emerged as a highly effective percutaneous technique for controlling obstetric and gynecologic hemorrhage. Uterine myomas are the most frequent cause of nonacute abnormal uterine bleeding. UAE is an effective therapy in the management of symptomatic myomas and may prove to be a valuable alternative to hysterectomy, myomectomy and medical therapy<sup>[26]</sup>. Since the introduction of uterine artery embolization as a minimally invasive treatment option for uterine fibroids, there has been a great deal of effort made toward developing other options for these patients. These options approach the problem differently, either with direct targeting of individual fibroids, organ-wide targeting of multiple fibroids, and systemic therapy to address the problem of fibroids using a hormonal approach. The primary candidates for this procedure include women who have symptomatic uterine fibroids who no longer desire fertility, but wish to avoid surgery or are poor surgical risks. The gynecologist is likely to be the primary initial consultant to patients who present with complaints of symptomatic myomas when hysterectomy is the only option,

UAE should be considered.<sup>[27]</sup> In order to completely block the arterial supply to the fibroid, UAE is typically performed in both uterine arteries. Different embolic agents are used such as polyvinyl alcohol, gelfoam and more recently gelatine tris-acryl microspheres. After UAE, perfusion of the uterus is maintained. Uterine function is therefore conserved and although women who become pregnant after UAE seem to be at risk for malpresentation, pre-term birth, cesarean delivery and postpartum hemorrhage, successful pregnancies after UAE have been reported in some series. A major technical problem with UAE remains the possible presence of fibroid blood supply from other sources, such as the ovarian arteries or other pelvic branches, which can lead to failure of the procedure. In conclusion, although randomized trials are still underway, UAE appears a good option for those patients who wish to conserve their fertility or when surgery is contra-indicated. However, to evaluate the long-term effects of UAE longer follow up is required.<sup>[28]</sup> UAE is a safe, well tolerated, and effective non-surgical treatment option for symptomatic uterine fibroids Good quality evidence supports the safety and effectiveness of UAE for women with symptomatic fibroids.<sup>[29]</sup> UAE is a safe, well tolerated, and effective non-surgical treatment option for symptomatic uterine fibroids.<sup>[30]</sup> This uterus-sparing procedure has low complication rates with excellent clinical outcomes and high patient satisfaction rates. The majority of women who undergo UAE report marked reduction in the severity of fibroid specific symptoms and significant improvement in their quality of life. In addition, it is associated with high risks of miscarriages, pre term delivery and postpartum bleeding. Generally, after UAE the recovery time and time lost from work are less; however, the potential need for subsequent surgery may be greater when compared with abdominal myomectomy.<sup>[31]</sup>

### **Transvaginal uterine artery occlusion**

Transvaginal Doppler-guided vascular clamp as a minimally invasive therapy for symptomatic uterine leiomyomas. The system is simple, easy to apply, and short-term efficacy may be equivalent to UAE is an alternative method of reducing blood flow in the uterine arteries for the treatment of uterine fibroids. It is based on the theory that fibroids are killed by temporary uterine artery occlusion through a mechanism of transient uterine ischaemia the procedure is performed by placing a Doppler ultrasound-enabled transvaginal clamp Systems. In the vaginal fornices and, guided by Doppler ultrasound

auditory signals, positioning it to occlude the uterine arteries by mechanical compression against the cervix. The clamp is left in place for 6 h and then removed. Potential advantages of this technique are no radiation exposure, no risk of non-target embolization, and the absence of significant post-procedure pain in most patients. However, although reported short-term results of transvaginal occlusion are similar to those of UAE, long-term outcomes might not be as favorable since the degree of tissue ischaemia affected by this procedure is dramatically less than with UAE. It appears, therefore, that long-term studies are needed to discern whether transvaginal uterine artery occlusion will lead to durable results, and to compare it with UAE. The system is simple, easy to apply, and short-term efficacy may be equivalent to UAE.<sup>[32]</sup>

### **Ultraminilaparotomy**

Ultra-minilaparotomy myomectomy with or without laparoscopic assistance might represent a safe and effective minimally invasive alternative to standard open myomectomy in the treatment of large myomas<sup>[33]</sup>. It may be a valid alternative in case of laparoconversion instead of the classic laparotomy approach.<sup>[34]</sup>

### **Robot-assisted laparoscopic myomectomy**

Robot-assisted laparoscopic myomectomy is a feasible technique for removal of deep intramural myomas unfavorably localized for traditional laparoscopy. The properties of the da Vinci robot facilitate dissection and suturing comprising the major surgical parts of myomectomy.<sup>[35]</sup>

### **Drugs under clinical trials**

#### **Fulvestrant**

Fulvestrant (Faslodex) is an estrogen receptor (ER) down regulator under development by AstraZeneca. Fulvestrant has potential in the treatment of other estrogen-responsive tumors, such as uterine tumors [178081]. By 1997, fulvestrant was in phase II trials for uterine fibroids [272162], and by February 1999, it was reported that phase II trials for endometriosis were ongoing [314472], [336599]. However, no development has been reported for these indications since that time. In October 2001, Morgan Stanley expected launch in 2002, with estimated sales of \$80 million in 2002 rising to \$208 million in 2007 [429700]. Analysts at Lehman Brothers predicted in December 2001, that

the product has a 90% chance of making it to market in 2002, with peak sales potential in this year of \$800 million (434768).<sup>[36]</sup>

### **Ulipristal**

HRA Pharma, under license from the Research Triangle Institute, is developing ulipristal, a progesterone receptor modulator, for the potential use as a contraceptive and an emergency contraceptive, and for the potential treatment of uterine fibroids. Phase II clinical trials for uterine fibroids and phase III trials for contraception are underway.<sup>[37]</sup>

### **CONCLUSION**

Uterine fibroids are common tumors and although benign they can be associated with significant morbidity. They may be encountered incidentally when performing imaging for other reasons and are usually easily recognizable. From the literature reviewed, it was obvious that the subject of uterine fibroid is still not fully exhausted. There is also the need to fashion out better treatment alternatives that will reduce morbidity in the process of managing the patient as well as those that will further enhance reproductive potentials after treatment.

### **REFERENCES**

1. Stanley J; Robboy; Rex C; Bentley; Kelly Butnor, and Malcolm C. Anderson. "Pathology and pathophysiology of uterine Smooth-Muscle Tumors" Environment Health Perspectives Supplements, October 2000, Vol-108, Number S5.
2. JAMA patent page, January 7 , 2009, Vol. 301, No.1.
3. Richard Enrique Blake, "Leiomyomata uteri: hormonal and molecular determinants of growth" Natl Med Assoc J, 2007 october,99(10), 1170-1184.
4. Radiological appearance of Uterine fibroids, year:2009, vol:19 ,issue:3, Page:222-231.
5. Yu L, Moore AB, Dixon D, Semin Reprod Med. "Receptor tyrosine kinases and their hormonal regulation in uterine leiomyoma" 2010 May, 28(3),250-9.
6. Schollmeyer T, Meinhold-Heerlein I, Walter C, Venhoff L, St Müller-Hülsbeck Ther Umsch. "Operative and interventional therapy of fibroids" 2007 Jul, 64(7),353-63.

7. Agdi M ; Tulandi T; Best Pract Res, Endoscopies management of uterine fibroids. Clin Obstet Gynaecol.J. 2008 Aug;22(4),707-16.
8. Trivedi P; Abreo M.“Predisposing factors for fibroids and outcome of laparoscopic myomectomy in infertility” Gynec Endosc Surg J. 2009,147-56.
9. Moorehead ME;Conard CJ; Ann N Y. “Uterine leiomyoma: a treatable condition” Acad Sci.J. 2001 Dec,948,121-9.
10. Bukulmez O; Doody KJ “Clinical features of myomas”. Obstet Gynecol Clin J. North Am. 2006 Mar,33(1),69-84.
11. J Gynec Endosc Surg “Predisposing factors for fibroids and outcome of laparoscopic myomectomy in infertility” 2009,1,47-56.
12. IpPP;Tse KY; Tam KF. Adv Anat Pathol J. 2010 Mar,17(2),91-112.
13. Bajekal N; Li TC Hum Reprod Update.“Fibroids, infertility and pregnancy wastage” 2000 Nov-Dec, 6(6),614-20.
14. Carol A. Anania, Elizabeth A. Stewart, Bradley “Expression of the fibroblast growth factor receptor in women with leiomyomas and abnormal uterine bleeding”J. Quade, Joseph A. Hill and Romana A. Nowak<sup>1</sup>, 1997, vol. 3 no. 8, 685-691.
15. R.FCasper.”Clinical uses of gonadotropin-releasing hormone analogues” CMAJ, 1991 January 15, 144(2, 153–158.
16. Environmental Health Perspectives.“Gonadotropin-releasing hormone agonists” June 2003, Vol.111,No. 8 ,1044.
17. Best Practice & Research Clinical Obstetrics & GynaecologyJ. “Gonadotrophin-releasing hormone analogues (GnRHa) therapy” August 2008, Volume 22, Issue 4, 655-676.
18. Subhuti Dharmananda, Ph.D., Director, Institute for Traditional Medicine, Portland Oregon “Chinese herbal therapy for Uterine Fibroids” September 2003.
19. Ligon AH; Morton CC. “Leiomyomata: heritability and cytogenetic studies” Hum Reprod Update. 2001 Jan-Feb,7(1),8-14.
20. Gordon P. Flake; Janet Andersen; and Darlene Dixon. “Etiology and Pathogenesis of Uterine Leiomyomas: A Review” Health Perspectives, June 2003, Vol.111, No. 8 ,1037.

21. Anthony N Griffiths<sup>1</sup>; Arianna; D'Angelo<sup>2</sup>; Nazar N Amso<sup>3</sup>; Griffiths AN; D'Angelo A; Amso NN. "Surgical treatment of fibroids for subfertility" Cochrane Database of Systematic Reviews 2006, Issue 3.
22. Marshburn PB; Matthews ML; Hurst BS "Uterine artery embolization as a treatment option for uterine myomas." *Obstet Gynecol Clin North Am.J.* 2006 Mar;33(1);125-44.
23. Moen MD; Noone MB; Elser DM "Natural orifice hysterectomy" *Urogynecology Network Int Urogynecol J Pelvic Floor Dysfunct.* 2008 Sep;19(9),1189-92.
24. Bajekal N; Li TC. "Fibroids, infertility and pregnancy wastage" *Hum Reprod Update.* 2000 Nov-Dec;6(6),614-20.
25. Cicinelli E; Tinelli R; Colafoglio G; Saliani N. Laparoscopy vs minilaparotomy in women with symptomatic uterine myomas: a prospective randomized s. *Minim Invasive Gynecol..j.* 2009 Jul-Aug;16(4),22-6.
26. Onder C; Seyma H; Kaya S. "Uterine artery Embolisation" *Indian J Radiol Imaging* 2002;12,67-9.
27. Siskin G; Tech Vasc "New treatments for uterine fibroids" *Interv Radiol.J.* 2006 Mar;9(1),12-8.
28. *European Journal of Radiology*, "Percutaneous uterine artery embolization for the treatment of symptomatic fibroids: current status" April 2005, Volume 54, Issue 1, Pages 136-147.
29. Giovanna Tropeano<sup>1</sup>; Sonia Amoroso and Giovanni Scambia. Non-surgical management of uterine fibroids Department of Obstetrics and Gynecology, Università Cattolica del Sacro Cuore, Largo Francesco Vito 1, 00168 Rome.
30. Judy Gainey Seals; Np; MSN (Cardiovascular Nurse Practitioner) <sup>1</sup> Paul A. Jones; MD, FACC, FACP (Chief of Cardiovascular Services, Mercy Hospital, and Medical Director; Jones Endovascular Institute) & Cheryl Wolfe, MD, FACOG (Teaching Faculty *CMAJ.* 1991 January 15;144(2), 153-158.
31. Uae Guidelines for the Management of Uterine Leiomyoma published by The Hong Kong College of Obstetricians and Gynaecologists. A Foundation College of Hong Kong Academy of Medicine , November 2009, No. 13.



32. Vilos GA ; Vilos EC ;Abu-Rafea B ;Hollett-Caines. Transvaginal Doppler-guided uterine artery occlusion for the treatment of symptomatic fibroids: summary results from two pilot studies” *Obstet Gynaecol Can.J.* 2010 Feb;32(2),149-54.
33. Ciavattini A; Tsioglou D; Litta P;Frizzo H;Tranquilli AL“Ultra-minilaparotomy myomectomy: a minimally invasive surgical approach for the treatment of large uterine myomas” *Gynecol Obstet InvestJ.* 2009,68(2):127-33. Epub 2009 Jul 8.
34. Ciavattini A ; Tsioglou D ;Tranquilli AL ; Litta P. Laparoscopic versus ultraminilaparotomic myomectomy for the treatment of large uterine myomas *Acta Obstet Gynecol Scand.J.*2010,89(1),151-5.
35. Lönnerfors C Persson. “Robot-assisted laparoscopic myomectomy; a feasible technique for removal of unfavorably localized myomas” *Acta Obstet Gynecol Scand.J.* 2009,88(9),994-9.
36. Johnston SR. Fulvestrant (AstraZeneca). *Curr Opin Investig Drug J.*2002 Feb,3(2),305-12.
37. Orihuela PA. “Ulipristal, a progesterone receptor antagonist as a contraceptive and for the treatment of uterine fibroids” *Curr Opin Investig Drugs.J.* 2007 Oct,8(10),859-66.

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