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# Myoma pseudocapsule – a biological and surgical structure to respect during myomectomy

Псеудокапсула миома – биолошка и хируршка структура коју треба поштовати током миомектомије

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# Myoma pseudocapsule – a biological and surgical structure to respect during myomectomy

Псеудокапсула миома – биолошка и хируршка структура коју треба поштовати током миомектомије

**Summary**
Uterine fibroids affect almost one in two patients, causing many pelvic problems and requiring pharmacologic and surgical treatment. For many years, the importance of the fibroid was emphasized as uterine pathology, without focusing on the complex myometrial biology peripheral to fibroid. Moreover, the traditional surgical technique in fibroid removal has not been investigated for years. In recent years, on the contrary, morphological, neuroendocrine and anatomical studies have demonstrated the importance of a biological and surgical structure surrounding myoma, rich in neurotransmitters and neurofibres, the myoma pseudocapsule. This structure is formed in the womb peripheral to fibroid onset, it separates the fibroid from the myometrium and acts as a tissue regenerator after removal of the fibroid from the uterus. The translation of scientific research on pseudocapsules into surgical practice has allowed us to identify new techniques of myomectomy, removing the myoma inside the pseudocapsule and promoting the pseudocapsules sparing surgery. All this to favor the subsequent biological process of uterine scarring and healing, by activating the neurotransmitters and neurofibres present in the myometrial fovea. The correct healing after fibroid removing restores the uterine anatomy, with a positive impact on subsequent reproductive function, reducing problems related to the muscle scar.
**Keywords:** myoma pseudocapsule; myomectomy; neurovascular bundle; reproductive surgery; pregnancy; fertility

**Сажетак**
Миоми материце се јављају код готово сваке друге болеснице, узрокују бројне интрапелвичне тегобе и захтевају фармаколошко или хируршко лечење. Дуги низ година, значај миома је посматран као болест материце, без фокусирања на комплексну билогију миометријума који их окружује. Уз то, традиционална хируршка техника уклањања миома није истраживана годинама. Насупрот томе, у новије време, морфолошке, неуроендокрине и анатомске студије су показале значај биолошке и хируршке структуре која окружује миом, богате неуротрансмитерима и нервним влакнима, односно псеудокапсуле миома. Ова структура се формира у материци периферно од миома, одваја миом од миометријума и функцинише као регенератор ткива након уклањања миома из материце. Пренос научних истраживања псеудокапсула у хируршку праксу омогућио је настанак нових техника миомектомије, које подразумевају уклањање миома унутар псеудокапсуле и промовисање поштедних операција у односу на псеудокапсулу. Све ово погодује накнадним биолошким процесима оживљавања и зарастања материце, активацијом неуротрансмитера и нервних влакана присутних у миометријалној ложи миома. Правилно зарастање након уклањања миома успоставља анатомију материце, са позитвним утицајем на касниј репродуктивну функцију, смањујући компликације повезане са ожиљком миометријума.
**Кључне речи:** псеудокапсула миома; миомектомија; неуроваскуларна петељка; репродуктивна хирургија; трудноћа; фертилитет



## INTRODUCTION

Uterine myomas, leiomyomas or fibroids are the most common pathology in female genital organs, most of them are asymptomatic, but they can cause severe symptoms [1]. The prevalence of uterine fibroids is ranging from 5.4% to 77% [2]. Fibroids negatively affect female reproductive function, as they are recognized as an important cause of infertility. Moreover, women affected by fibroids are at higher risk for complications during pregnancy, labor, and delivery [3]. Fibroids are preferentially treated by surgery, by vaginal, laparoscopic, laparotomic or hysteroscopic approach [4, 5, 6].

Currently, minimally invasive techniques based on biologically reasoned myomectomy allow the preservation of the myoma pseudocapsule, in order to spare the muscular and fibro-

 

neurovascular myometrial fibers, ensuring the complete and bloodless removal of the myoma [7, 8].

## PHYSIOLOGY OF UTERINE MUSCLE REPAIR

Myometrial scar after myomectomy requires a correct and physiological healing. The healing process, once the fibroid is enucleated, is one of the fundamental steps that restore uterine reproductive function. Nevertheless, the muscle damage itself may promote the signaling activities to trigger regeneration of the myometrium. The synthesis and release of signaling molecules, initiated by neurotransmitters and neurofibres, after the cellular damage, can prompt itself the cell activation, inducing muscle regeneration and healing [9]. After the muscle damage, the biological sequence "injury-repair-regeneration" leads to complete functional recovery during the days or weeks after the initial injury [10].

A fundamental process in the regeneration of a damaged muscle is the revascularization of the injured muscular tissue. The neoangiogenetic network in the myometrial fovea (where the fibroid was located) is the first mark of tissue repair, as a necessity for the later morphological and functional healing. New capillaries grow from the surviving stems of the blood vessels into the center of the myometrial fovea; the neoangiogenesis in the damaged myometrium provides a sufficient supply of oxygen, improving aerobic energy metabolism for the muscular tissue repair [11]. In such regenerative process, the neuropeptides and neurotransmitters have an significant role in wound healing. Moreover, there is proof that the nervous system and its neurotransmitters, such as neuropeptide Y (NPY), Substance P (SP), Vasoactive Intestinal Peptide (VIP), Oxytocin, Vasopressin (VP), growth hormone-releasing hormone (GHRH), protein gene product 9.5 (PGP 9.5) and calcitonin gene-related peptide (CGRP) play a crucial role in mediating inflammation and healing processes [9, 12, 13]. Among these neurotransmitters, it has been demonstrated a slight distribution of oxytocin neurofibers into the uterus, with their high presence into the cervico-isthmic area [14].

Analyzing the biology of the myometrial scar after myomectomy, the spared neuropeptides enhance the correct myometrial healing at hysterotomic site and most of the above-mentioned neuropeptides have been found in the fibroid pseudocapsule, as a neurovascular bundle surrounding fibroid [14–17]. Until today, it has not been possible to clarify if the pseudocapsule vasculature network could be or sustained by mechanical and



 

inflammatory effects of fibroid on myometrium, or produced by a sort of "neoplastic-type" neoangiogenesis, due to the myoma growth or even to a muscle and tissue healing process [18].

In human uterus, obstacles in attaining serial specimens of hysterotomic scar after myomectomy are the main problems of biological and surgical investigations. Thus, the post-cesarean section and post-myomectomy remodeling processes in the womb are currently an unsolved puzzle. They can be monitored only by ultrasound (US) or magnetic resonance imaging (MRI) [19].

Healing of the wound is a vibrant process which involves neuromediators, neuropeptides, angiogenetic factors, blood cells, extracellular matrix and parenchymal cells. It follows three composite and coinciding phases: inflammation, tissue formation and remodeling [20]. In these phases, the intra pseudocapsule growth factors can be very useful in the enhancing the muscle repair process after myomectomy [21].

Anyway, the biogenesis of myoma pseudocapsule requires further investigations, either on the analysis of the hormonal and pharmacological effects of drugs on pseudocapsule, based on reducing fibroid growth without compromising pseudocapsule characteristics [22], or on the pre-operative therapy and the post-operative follow up, in order to preserve womb functionality, as much as possible [23].



## THE "INTRACAPSULAR MYOMECTOMY"

The rationale for the fibroid removal starts with the preservation of its pseudocapsule (Figure 1.), the neurovascular bundle which surrounds myoma itself [15, 16, 17]. This modern technique of removing fibroids was adapted from the urology, in which the removal of the prostate gland must occur with the conservation of the neurovascular bundle above it. Thus, concerning the significance of the prostatic capsule sparing and the physiological role of nerve-sparing techniques for prostatectomy, it was possible to translate it on the pseudocapsule sparing during myomectomy.

There are also some passages that can be borrowed from urology to gynecology during prostatectomy and myomectomy. During laparoscopic/robotic prostatectomy, if bleeding

 

occurs, insufflation pressure can be in the meanwhile increased and a local compression can be performed also by hemostatic gauze, directly on prostate neurovascular bundle (the source of bleeding). The same surgical passages can be repeated during laparoscopic myomectomy (Figure 2.), in case of bleeding. Then, the hemostasis by high wattage diathermocoagulation should be always avoided during dissection near the prostate neurovascular bundles, as it has been shown that it can be harmful to cavernous nerve function in the canine model, with an indirect damage of the pelvic nerves of sexual function after prostatectomy [18, 24].

Returning to the fibroid enucleation technique, the possibility to perform myomectomy by removing the myoma from its pseudocapsule, was called "intracapsular myomectomy" [16, 18, 19]. In this technique, fibroid is carried out, by surgeon, from its muscular fovea, by stretching and enucleating myoma directly from the adjacent myometrium, avoiding the damage of the adjacent fibromuscular skeleton, breaking up the fibrous bridges (Figure 3.) [4, 6, 25, 26]. As a general surgical recommendation, in robotic, laparoscopic, laparotomic, vaginal or hysteroscopic setting, the surgical enucleation of each fibroid needs to be gently performed always to enhance and to improve the successive myometrial healing, trying to correctly restore the uterine anatomy and biology [27, 28]. Thus, the myoma pseudocapsule neurovascular bundle needs to be preserved and spared during myomectomy, avoiding any damaging surgical maneuvers, such as extensive and high wattage diathermocoagulation or unnecessary tissue manipulation or muscular injury. This physiological surgical technique to remove fibroids largely respects the fibroid neurovascular bundle, and its neuropeptides and neurofibers, since the iatrogenic pseudocapsule damage may change the successive neurotransmitters function in muscle repair, thus impairing uterine healing [8, 18].

The operative consequences of an inappropriate myomectomy technique performed with pseudocapsule injuring may lead to: 1) a reduction in the number of neuropeptides and neurofibers at hysterotomic site, with a negative impact on physiological myometrial healing; 2) an increase of fibrotic process at hysterotomic site; 3) a insufficiency either of myometrial neurotransmission or of muscular impulse and contractility. All of these features can lead to an altered post-surgical uterine physiology, as well as to a reduced uterine musculature functionality. This process could be the main responsible of impaired healing with uncorrected myometrial functionality, with unfavorable effects on a subsequent pregnancy, including a possible dramatic uterine rupture [29, 30].



 

## LAPAROTOMIC/LAPAROSCOPIC INTRACAPSULAR MYOMECTOMY

The laparotomic and laparoscopic intracapsular myomectomy techniques do not differ substantially, except for the major surgical benefit of laparoscopy in case of subserous and intramural fibroids. The principal benefits of the endoscopic approach are the significant reduction of perioperative operative blood loss, the lower requiring of analgetic drugs and the shorter hospitalization. Additionally, laparoscopic intracapsular myomectomy results in slightly enhanced short-term outcomes in terms of postoperative fever, myometrium scar hematoma formation, ileus and antibiotic treatment, in comparison to laparotomic surgery (Figure 4.). The laparoscopic myomectomy has a reduced blood loss for the haemostatic CO2 pressure, a part the selective gentle coagulation of pseudocapsule vessels. The CO2 insufflation can reduce blood loss during laparoscopy, as the increased intra-peritoneal pressure can lead to the occlusion of the small blood vessels and capillaries during myomectomy [30]. This effect, in combination with a combined with a fewer traumatic endoscopic micro-manipulations, could result in overall positive surgical results [2, 7, 25].

Once the visceral peritoneum is incised in the midline longitudinal plane, by monopolar scissors, by Harmonic scalpel, monopolar scissors or crochet needle electrode, the myoma pseudocapsule is easily recognized during dissection and then cut to expose the fibroid surface. The identification of the “cleavage plane” between fibroid and pseudocapsule is important for a correct intracapsular myomectomy, in order not to preserve muscular fibres and to selectively coagulate blood vessels of pseudocapsule. Atraumatic clamp or irrigator cannula should be used to gently dissect myoma from its pseudocapsule. Hemostasis of the small vessels bleeding can be selectively achieved by a low wattage bipolar clamps, Harmonic scalpel, hook electrode or monopolar scissors, always at low wattage (not more than 30 watts), to progressively expose the hidden part of the fibroid into uterus (the myometrial fovea), incorrectly called “the base of the myoma”, and the pseudocapsule fibrovascular bridges (selectively coagulated). This technique allows a complete minimally traumatic removal of the fibroid from its pseudocapsule, with a minimal blood loss and a pseudocapsule sparing.



 

## HYSTEROSCOPIC INTRACAPSULAR MYOMECTOMY

The rise of hysteroscopic myomectomy in 1976 [31] represented a revolution in the treatment of submucous fibroids: It allowed the abandonment of the laparotomic approach, significantly improving patients' surgical outcomes. Nowadays, the hysteroscopic myomectomy represents the gold standard in treatment of submucous myomas [32]. Nevertheless, the submucous myomas treatment is probably the high risk hysteroscopic procedure than other, for potential complications it has, as cervix laceration, hemorrhage, uterine perforation or clinical intravasation syndrome [33, 34]. It is not easy to estimate the right frequency of the abovementioned complications as it is of high variability according to pathology characteristics, surgeon skills and employed technique [35].

Wamsteker [36] and Lasmar [37] investigated and assessed the characteristics of submucous fibroids able to influence surgical outcomes in hysteroscopic myomectomy. The treatment of intracavitary fibroids with an intramural extension of 50% or more has always been represented as a challenge for the hysteroscopic surgeons, as it is burdened by an increasing risk for intraoperative complications, sometimes requiring a multiple-step procedure [5, 36, 38]. Moreover, in cases of multiple myomas, the risk it is even higher.

Currently, resectoscopic slicing still is the most commonly used technique for treating submucous myomas, and probably for this reason, myomectomy represents the hysteroscopic procedure with a higher complication rate. Unfortunately, the classical slicing technique, even in expert hands, does not respect the pseudocapsule and the adjacent healthy myometrium. During the resection of the intramural component of myoma, the "pseudocapsular tissue" should be visualized all over the resected area. Sometimes, for fibroid dimension and bleeding it can be challenging to make a distinction between the myoma tissue, the pseudocapsule and the healthy myometrium. The problem is the direct action of electrical loop during the myoma slicing and the uncorrect dissection of the anatomical planes. The traditional technique altered the intrauterine anatomy and it is almost impossible to avoid the injury of the myometrial fibers, causing a direct (by cutting) and indirect (by thermal spreading) damage of the pseudocapsule and surrounding healthy myometrium. This fundamental issue is responsible for all the intraoperative complications during the hysteroscopic myomectomy. Moreover, the role of surgical trauma to the healthy myometrium during hysteroscopic surgery can lead to synechiae and adhesions formation [28, 39].

The ideal hysteroscopic myomectomy ideally should be performed in one surgical step, as safe and effective procedure, which is simple and well-tolerated [32]. In the last decades, several techniques have been proposed, in order to overcome the limits represented by the classical slicing for the treatment of the myometrial portion of submucous myomas [5]. The main objective of these techniques was the detachment of the intra-myometrial part of the fibroid, in order to enable the sliding from the myometrium into the uterine cavity. Some authors proposed the use of uterine contractions, induced by manual massage [40], drugs [41, 42] or changing intrauterine pressure [43]. A combination of multiple techniques and the US monitoring during myomectomy was also described [44, 45]. Authors proposed the detachment of intramural component of fibroids by electrical incision of the fibroconnectival bridges, anchoring myoma to the pseudocapsule [46].

A technique that allowed us to overcome the limits represented by the classical slicing was described in 1995, as the cold loop hysteroscopic myomectomy [46]. This method allowed to change the approach to the myoma, from the progressive reduction or electrical power using and its switching to a mechanical enucleation of the myoma from the pseudocapsule, by the physiological contraction of myometrium. It represented a revolution in the hysteroscopic treatment of submucous fibroids, since it distinguished the anatomical planes, respected the anatomical and functional integrity of the myometrium and of the pseudocapsule, while at the same time ensuring a safe and effective procedure. By the cold loop myomectomy, the fibroconnective bridges that anchor the myoma to its pseudocapsule are mechanically disconnected, enucleating the intramural component of fibroid, without any effect to the adjacent healthy myometrial tissue. Moreover, the cold loops are applied between myoma and pseudocapsule, allowing to avoid uterine perforation by electrical loop and injury to abdominal organs or vessels. Noteworthy, in case of perforation by cold loops, the damage induced can be considered as the same with a Hegar dilator [8].

Finally, the respect of the myometrium allows uterine contraction, facilitating the sliding of the intramural part of the fibroid in the uterine cavity and at the same time increases the free myometrial margin thickness [47]. The uterine contraction and the respect of the myometrial muscular fibers decreases the risk of bleeding and the absorption of the distension medium, enhancing the possibility to accomplish the treatment in a single operation [48].



 

The respect of the pseudocapsule promotes the myometrial better healing, avoiding scarring and reducing the intrauterine adhesions and dramatic complications, such as subsequent uterine rupture [5, 28, 49, 50].

## CONCLUSION

The morphological and molecular investigation performed on fibroid pseudocapsule changed the current surgical and biological scenario of myomectomy, for their interesting scientific results. The discovery of the fibroneurovascular structure surrounding fibroid, rich in neuropeptides and neurotransmitters, translated the new concept of myomectomy in reproductive surgery and in fertility sparing procedures, even for giant fibroids and during pregnancy.

Many evidences on the presence of angiogenetic proprieties in few millimeters of biological structure, the pseudocapsule, underline the necessity to preserve it as much as possible while performing myomectomy, especially to preserve myometrial integrity nearby the fibroid site, indirectly enhancing myometrial healing after myomectomy, and for less surgical bleeding.

Intracapsular myomectomy should also enhance the post-operative adhesions reduction. In our opinion, the intracapsular myomectomy, with a pseudocapsule sparing by endoscopic "microsurgical" magnification, as a safe and feasible minimally invasive technique, should be reproduced in all myomectomies.

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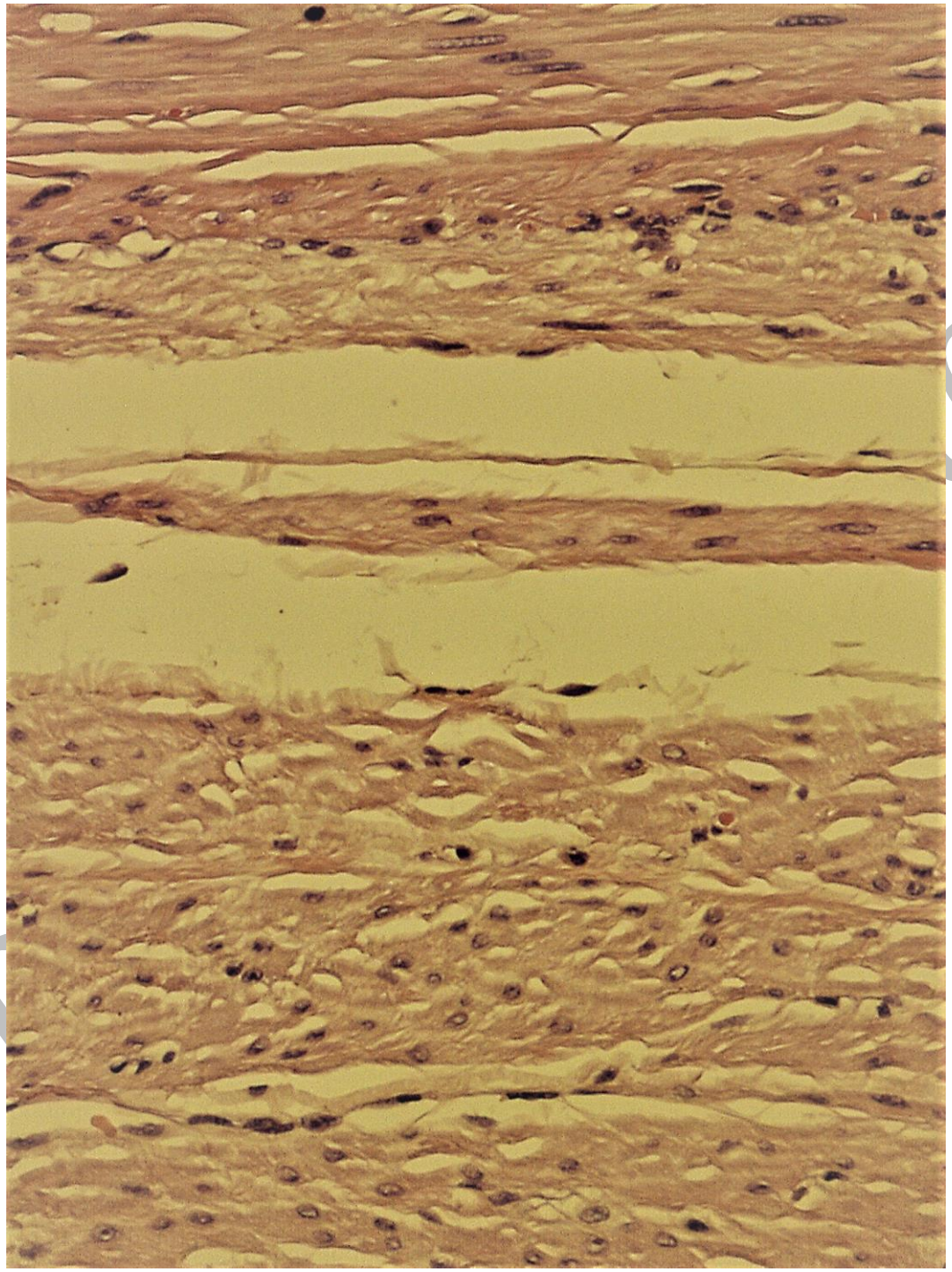

**Figure 1.** Hystology of myoma pseudocapsule

 

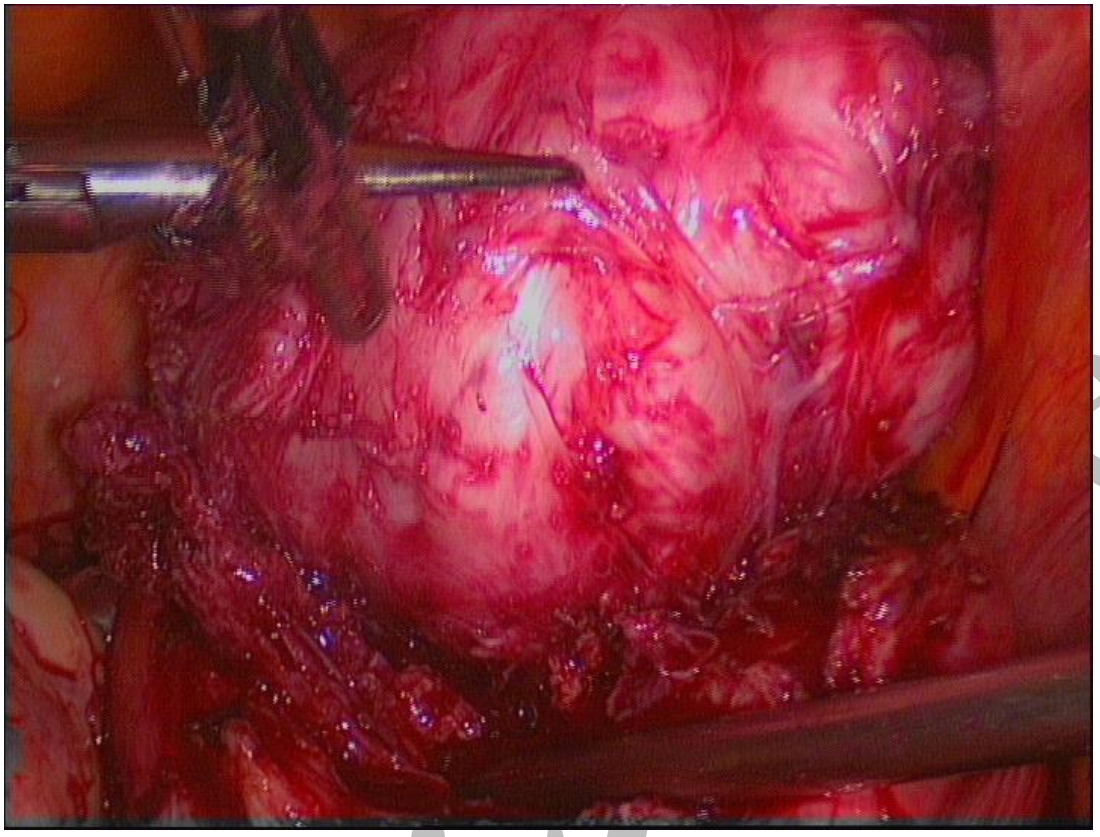

**Figure 2.** Laparoscopic intracapsular myomectomy



 

**Figure 3.** Macroscopic exposition of pseudocapsule



 

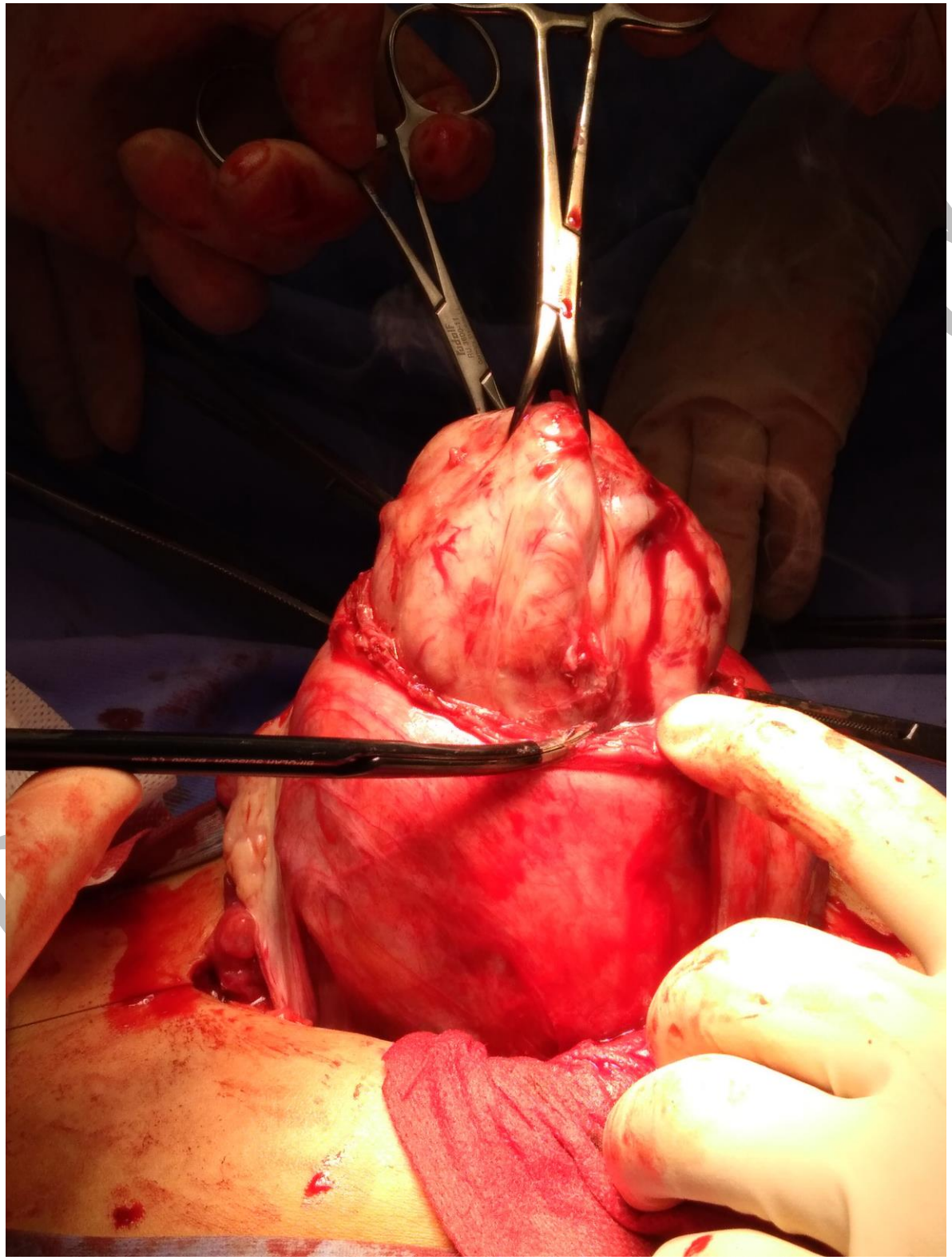

**Figure 4.** Laparotomic intracapsular myomectomy

 