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# Pelvic lymphedema in rectal cancer: a magnetic resonance feasibility study: a preliminary report

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**Abstract. – BACKGROUND: Functional pelvic disorders in patients undergoing conservative surgical approach for rectal cancer are considered a major public health issue and represent one third of cost of colorectal cancer. We investigated the hypothesis that lymphadenectomy, involves the pelvic floor results in a localized hides or silent pelvic lymphedema characterized by symptoms without signs.**

**PATIENTS AND METHODS: We examined 13 colo-rectal cancer patients: five intra-peritoneal adenocarcinoma: 1 sigmoid and 4 upper third rectal cancer (1 male and 3 female) and 9 extra-peritoneal adenocarcinoma: 3 middle and 5 lower third rectal cancer (4 male and 5 female) using 1.5-T magnetic resonance, one week before and twelve months after discharged from hospital.**

**RESULTS: Lymphedema was discovered on post-operative magnetic resonance imaging of all 9 patients with extra-pertitoneal cancer, whereas preoperative magnetic resonance imaging as well as a post-operative examination of 4 intra-peritoneal adenocarcinoma, revealed no evidence of lymphedema. Unlike the common clinical skin signs that typify all other sites of lymphedema, pelvic lymphedema is hides or silent, with no skin changes or any single symptom manifested. Magnetic resonance imaging showed that pelvic illness alone is accompanied by lymphedema related exclusively to venous congestion, and accumulation of liquid in adipose tissue or lipedema.**

**CONCLUSIONS: Alteration of the pelvic lymphatic network during pelvic surgery can lead to lymphedema and, pelvic floor disease. Patients should be routinely examined for the possibility of developing this post-surgical syndrome and further studies are needed to establish diagnosis and to evaluate treatment preferences.**

*Key Words:*
Lymphedema, Rectal cancer, Pelvic dysfunction.

## Background

The prognosis for pelvic malignancies has improved in recent years mainly due to advanced technologies and better knowledge of the pathways of cancer spread. Lymphadenectomy is the most important prognostic factor in pelvic malignancies, a finding that has substantially changed surgical approaches from a quantitative premise to a more qualitative nature giving priority to the psycho-physical integrity of cancer patients by limiting the surgical intervention[1-4].

However, despite progress made by the conservative surgical approach for rectal cancer, the development of functional abnormalities in patients undergoing conservative surgery has become more evident[5]. These functional pelvic disorders are associated with symptoms similar to those of the pre-surgery pelvic pathology. Most importantly these problems are considered a major public health issue representing one third of costs of colorectal cancer treatment, even if the massive economic burden of disability has received limited attention[6]. Although these theories including neural damage, reduction of capacity and compliance of organs, and sensory loss have been already proposed, no clear evidence of a direct correlation between such symptoms and surgical damage exists. Additionally, such disabilities do not depend on the extent of the surgical intervention (conservative versus radical), on the use of concomitant post-operative radio-chemotherapy or gender[7]. Fortunately, patients have been shown to respond to biofeedback re-education of the pelvic floor, with or without added psychotherapy[8].

We hypothesized that pelvic surgery, regardless of the extra-peritoneal organs, results in the loss of continuity of the pelvic region, as key event with the following reduction in fatty tissue where the lymph node stations are mostly concentrated[9]. Therefore, we suggest that pelvic lymphadenectomy should be followed by a pelvic lymphedema[9]. Once identified, lymphedema does not undergo significant reabsorption and may lead to serious chronic pathology with severe functional impairment of pelvic organs. Yet,

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the mechanisms and pathways that involve lymphedema in pelvic pathology are still unknown and need to be investigated. We examined, by chance, post surgery lymphedema in 13 patients submitted to hospital for colorectal adenocarcinoma, by comparing magnetic resonance (MR) of the abdominal area of the pre and post surgery. The relationship between MR and lymph node staging in rectal cancer renders it conceptually appealing to pursue pelvic mapping[10]. Realizing the opportunities and challenges of pelvic mapping, this preliminary report investigates the feasibility of MR imaging and examines its applicability for pelvic lymphedema. At the best of our knowledge, this is the first study on pelvic phenomena's after rectal surgery. The strong evidence using MRI to demonstrate the presence of pelvic lymphedema after rectal surgery, convinced us to publish this pilot study.

In our case load we currently observed functional pelvic disorders associated with symptoms similar to those of the pre-surgery pelvic pathology in patients submitted to anterior resection of the rectum. To discriminate supposed pelvic lymphedema, we compared the extra-peritoneal adenocarcinoma with intra-peritoneal adenocarcinoma. Data was obtained by chance from patients admitted to IRCCS Foundation "National Institute of Tumors" of Milan, between May 2008 and January 2010. Excluded from the analysis were patients with preoperative treatment (radiochemotherapy), those patients with loco-regional recurrence, previous pelvic surgery or patients with distant metastases and with more than one primary cancer. We regarded the rectum cut-off within 15 cm from the anal verge and intra-peritoneal cut-off more than 12 cm from the anal verge. We identified 13 patients with sigmoid colon and rectal adenocarcinoma. Bowel preparation and surgical techniques have been described in details by Leo et al[11]. All patients had a pre-operative (one week before surgery) and post-operative (twelve months following discharge from the hospital) MR examination. This study was approved by the Institutional Review Board.

## Patients and Methods

### MR

In details, a 1.5-T high-resolution MR imaging system (Avanto; Siemens Medical Systems, Erlangen, Germany) was used for the pre operative stages and the follow-up of the patients. For the purpose of our preliminary report, the 13 patients were examined in the supine position with feet forward and measurements were obtained using the same system and by the same technician.

We consider the common features of lymphedema, usually observed in an MR examination: circumferential edema, increased volume of subcutaneous tissue, and a honeycomb pattern above the fascia between muscle and subcutaneous fat, with evident thickening of the dermis[12]. Although it is generally difficult to differentiate primary from secondary lymphedema, MR is able to discriminate lymphedema from lipoedema and phlebedema[13,14]. Our standard procedure for pre-operative patients is an MR with Gadolinium. On the other hand, for follow-ups, the MR is indicated only for a suspicious local recurrence. Thirteen patients were selected for our study to be evaluated with MR but with a different approach. In details, along with the above described standard procedures, a sequence of fat-suppressed T2-weighted (FST2) and diffusion weighted T2-weighted (DWIT2) were performed, as those are the most efficient techniques to evaluate lymphedema. We considered the protocol for DWI-MR of the pelvis proposed by Mir et al[15]. Specifically, to evaluate lymphedema using FST2 the signal should be increase as the presence of increasing degrees of edema related to active inflammation[15]. Additionally, DWIT2 has been found to improve the detection of edema and herein introduced to detect the lymphedema degree[16]. Moreover, when lipoedema occurs MR is able to confirm that the peripheral lymphatic system is normal while soft tissue swelling consists solely of fat, and subcutaneous edema is absent. Criteria for evaluation of the MRI provided two reviewers, they were blinded with respect of clinical data.

## Results

The data regarding thirteen patients admitted to our Department for colo-rectal adenocarcinoma are reported. Table I summarizes surgery information for each patient. Five were males and 8 females with a median age of 66, ranging from 45 to 72 years. In all patients, a whole body mass index (BMI) was calculated: range 25-35, mean 29.9.

Cases included patients with adenocarcinoma of the sigmoid colon without metastases and of the rectum without metastases. Four patients

**Table I.** Characteristics of patients from May 2008 to January 2010.

| Number patient | Age | Sex | Body mass index | Site of cancer | Surgical procedure | Cancer classification |
|---|---|---|---|---|---|---|
| 1 | 45 | Female | 25 | Sigmoid colon | RSC | IIa |
| 2 | 72 | Male | 35 | URC | ARR | IIa |
| 3 | 68 | Female | 31.6 | URC | ARR | IIa |
| 4 | 70 | Female | 25.8 | URC | ARR | I |
| 5 | 55 | Female | 29.9 | URC | ARR | I |
| 6 | 60 | Male | 28.8 | MRC | ARR | I |
| 7 | 59 | Female | 29.6 | LRC | ARR | IIa |
| 8 | 71 | Female | 29.9 | LRC | ARR | I |
| 9 | 66 | Male | 28.9 | MRC | ARR | I |
| 10 | 65 | Female | 31.2 | MRC | CEAA | IIa |
| 11 | 64 | Female | 33.5 | LRC | ARR | I |
| 12 | 67 | Male | 34.5 | LRC | CEEA | I |
| 13 | 67 | Male | 33.3 | LRC | ARR | I |

Upper third rectal cancer (URC), Middle third rectal cancer (MRC), Low third rectal cancer (LRC), Resection of the sigmoid colon (RSC), Anterior resection of the rectum (ARR), Total resection of the rectum with colo-endo anal anastomosis (CEAA). Cancer classification with American Joint Committee on Cancer Staging 2010.

have been affected by intra-peritoneal adenocarcinoma: one sigmoid and 3 upper third rectal cancer (1 male and 3 female) and 9 extra-peritoneal adenocarcinoma: 4 middle third rectal cancer and 5 lower third rectal cancer (4 male and 5 female). The patients affected by intra-peritoneal adenocarcinoma have been submitted to: one resection of sigmoid colon and 3 anterior resection of upper rectum. Specifically, 3 patients presented stage IIa and one stage I. The patients affected by extra-peritoneal adenocarcinoma have been submitted to 7 anterior resection of the rectum and 2 total resection of the rectum with colo-endo anal anastomosis. In details, 7 patients presented stage I and 2 stage II.

Nine patients with an extra-peritoneal lesion underwent a resection of middle and lower third of rectum with regional lymphadenectomy, while the other patients with an intra-peritoneal lesion required resection of sigmoid colon and upper third of the rectum with regional lymphadenectomy.

Table II summarizes the characteristics for each patient using 4 paramenters: stipes-like, edema and venous congestion, epifascial "lakes", lymphatic stasis in presacral space. A sagittal and coronal T1 MR, as well as FST2 and DWIT2 images on the axial plane were requested for the 7 patients who underwent anterior rectal resection, which involved the pelvic floor, as a result of ex-

**Table II.** MR characteristics.

| | Stipes like | | Edema and venous congestion | | Epifascial lakes | | Lymphatic stasis in presacral space | |
|---|---|---|---|---|---|---|---|---|
| Patient | MR pre | MR post | MR pre | MR post | MR pre | MR post | MR pre | MR post |
| 1 | No | No | No | No | No | No | No | No |
| 2 | No | No | No | No | No | No | No | No |
| 3 | No | No | No | No | No | No | No | No |
| 4 | No | No | No | No | No | No | No | No |
| 5 | No | Yes | No | Yes | No | Yes | No | Yes |
| 6 | No | No | No | Yes | No | Yes | No | Yes |
| 7 | No | No | No | Yes | No | Yes | No | No |
| 8 | No | Yes | No | Yes | No | No | No | No |
| 9 | No | Yes | No | Yes | No | Yes | No | Yes |
| 10 | No | Yes | No | Yes | No | Yes | No | No |
| 11 | No | Yes | No | Yes | No | Yes | No | Yes |
| 12 | No | Yes | No | Yes | No | Yes | No | Yes |
| 13 | No | Yes | No | Yes | No | Yes | No | Yes |

tra-peritoneal location of the adenocarcinoma (middle and lower third of the rectum). There is no clear evidence of the pelvic lymphedema or lymphatic alterations in the pre-operative MR performed 1 week prior to surgery for all patients (Figure 1). However, a post-operative MR follow-up performed 12 months flowing discharge from the hospital revealed in 7 patients a lymphatic "stipes-like" elements within the presacral adipose tissue with compression of the sacro-sciatic ligaments and bladder, all indicative of lymphatic alterations (Figure 2). Moreover in 9 patients, the area of edema and venous congestion of pelvis together with compression of pelvic organs indicated by MR signals, were located far from the area of surgical intervention (Figure 3). Furthermore, in 8 patients, with the phase of T1 acquisition, epifascial lakes related to the muscular bands located outside of the pelvic floor in gluteal muscles were identified (Figure 4). Additionally, in 6 patients, the DWIT2 enabled the detection of moderate lymphatic stasis in the presacral space (Figure 5).

The 4 patients who underwent resection of the sigmoid colon and upper third of the rectum (without pelvic involvement due to intra-peritoneal adenocarcinoma located more than 12 cm from the anal verge), had a different MR outcome. In details, the axial second planes were amplified with acquisition of T1, FST2 and DWIT2-weighted sagittal and coronal images through subtraction of adipose tissue signals on the axial planes. Pre-operative MR revealed no pelvic lymphedema or alterations of the pelvic lymphatics in these patients.

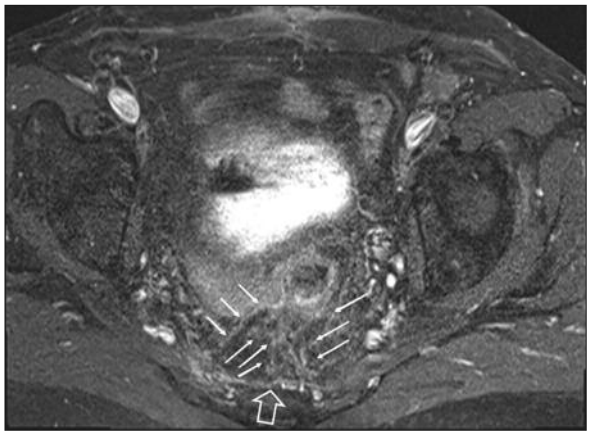

**Figure 2.** Post-operative period. Phase of FST2 acquisition. White arrows indicate lymphangitis in the sacral area; large open arrow indicates presacral fibrosis. (Patient number 9).

Also the post-operative follow-up performed twelve months after discharge from the hospital, showed no evidence of pelvic wall edema. Two patients (number 1 and 4), submitted to resection of the sigmoid colon, presented mild signal intensification in the lower part of the rectal abdominal muscle (Figure 6). Overall, there are no signs of lymphatic congestion anywhere within the pelvic wall were noted in the four patients with intra-peritoneal surgery.

## Discussion

The strong evidence using MRI to demonstrate the presence of pelvic lymphedema after rectal

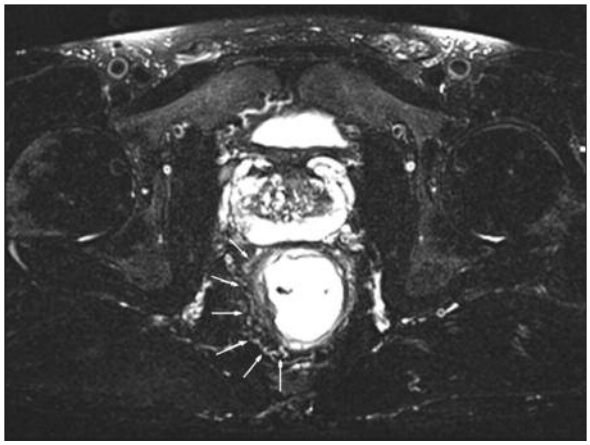

**Figure 1.** Phase of FST2 acquisition in pre-operative period, revealing no evidence of lymphedema. White arrows indicate the primary lesion. (Patient number 12).

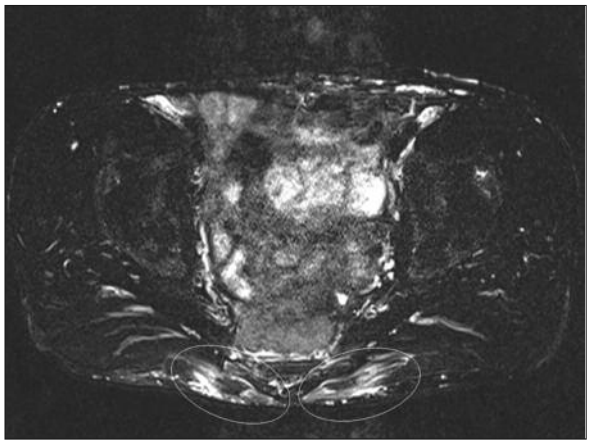

**Figure 3.** Post-operative period. Phase of FST2 acquisition. Note lymphedema and venous congestion post to the sacral area. (Patient number 6).

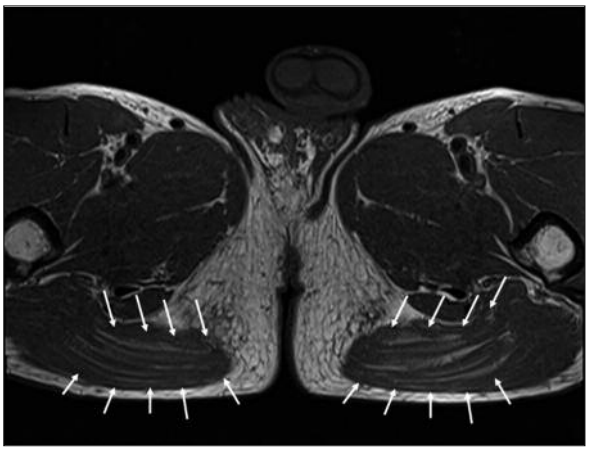

**Figure 4.** Post-operative period. Phase of T1 acquisition. Arrows surrounding muscular fascia indicate the epifascial lakes. (Patient number 13).

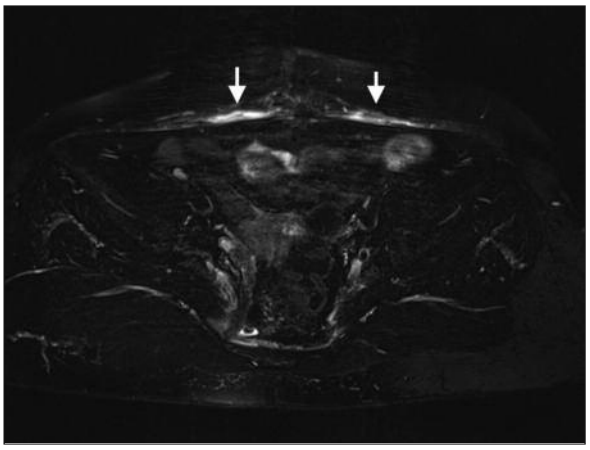

**Figure 6.** Post-operative period. Phase of FST2 acquisition. Arrows indicate mild hyperintensity in the area of abdominal rectal muscles. (Patient number 2).

surgery, convinced us to publish this report. In this study using abdominal MR we hypothesized that pelvic surgery, regardless of the extra-peritoneal organs, results in the loss of continuity of the pelvic region as key event with the following reduction in fatty extra-peritoneal tissue where the lymph node stations are mostly concentrated; the consequent pelvic lymphadenectomy, should be followed by a pelvic lymphedema[9]. As lymphedema been discovered often by chance and has no reported common elements, it has been difficult to create an experimental model[17]. Here, we attempted to generate a diagnostic model by exploiting the radiological resources available in our laboratory. The relationship between MR and lymph node staging in rectal cancer renders it conceptually appealing to pursue pelvic mapping[10]. Realizing the opportunities and challenges of pelvic mapping, this work demonstrates the feasibility of MR imaging and examines its applicability for pelvic lymphedema even with a small number of patients. Criteria for evaluation of the MRI studies provided two reviewers, they were blinded with respect of clinical data. We didn't performed inter observer variability between readers.

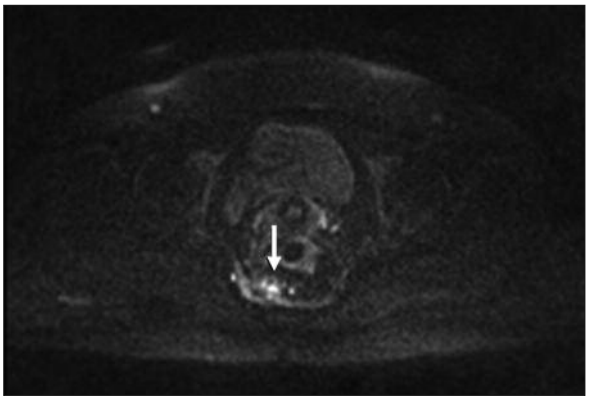

**Figure 5.** Post-operative period. Phase of T2WI. Arrow indicates lymphedema in the presacral space. (Patient number 7).

Lymphedema results from an alteration of lymphatic vessels as a consequence of malformation (primary) or mechanical damage (secondary), consistent with an equal distribution in the upper and lower limbs, neck, scrotum and pubis[18-20]. Analogously, pelvic lymphedema might be a consequence of mechanical pelvic injury or of the altered lymphatic system caused by such injury. The extra-peritoneal pelvic area is sited between the peritoneum covering the pelvic organs, and the pelvic diaphragm. In the pelvic cavity the peritoneum is separated from the walls which delimit the cavity by the surrounding and supporting fatty extra-peritoneal tissue. Pelvic lymphadenectomy might in itself lead to damaged lymphatic vessels with subsequent pelvic malfunction, within a few weeks post surgery if undiagnosed and untreated, can progress to a chronic pelvic dysfunction. Our post-operative MR evidenced injuries involving different pelvic structures and areas, whereas no venous congestion or alteration of lymphatic vessels was detected preoperatively (Table II). Therefore, it is of critical importance to investigate the mechanisms of lymphedema in pelvic pathology to limit the damages of functional abnormalities in patients who undergo conservative surgery.

Thus, despite the benefits of surgery, our findings support the notion that lymphadenectomy can cause damage of the pelvic lymphatic system as a direct result of surgery. Unlike the common clinical skin signs that characterized all other sites of lymphedema, pelvic lymphedema is hidden or silent, with no skin changes or any single symptom manifested[9]. The lack of signs is not surprising, considering that the shell structure of bones of the sacral area provides a structural system capable of containing almost three-fourths of the total volume alterations inside the pelvis without any external manifestations. Moreover, the perineum, which contains no bone structures and thus enables direct and unrestricted internal pelvic communication, is particularly vulnerable to damage caused by lymphadenectomy. This alteration of lymphatic vessels would produce lymphedema or progressive functional pelvic disorders manifesting as muscular deficiency, particularly defective sphincter control. As shown in our MRs of the bone-tendineal space interposed within a deep plane of the pelvic floor, surgical intervention involving perineal skin hidden lymphedema, despite the lymphatic congestion after lymphadenectomy and eventually the conditions for neural and muscular structural malfunction[21,22].

The use of MR has made it possible to emphasize the pre-operative period in which the presence of the cancer is not associated with any pelvic lymphedema. Moreover, our MRs showed that pelvic illness alone is accompanied by lymphedema related exclusively to venous congestion, which can be attributed to the neoangiogenesis typically concurrent in these carcinomas. In the post-operative period the effects of lymphadenectomy and opening of the pelvic peritoneum are characterized by specific signs of lymphedema, such as lymphangitis with local fibrosis formation. Actually, the identification of epifascial lakes over gluteus muscles in the absence of edema inside of the muscular girdles demonstrates that surgical intervention sets off a domino effect within the pelvic area. The hyperintense regions within the gluteus muscle are usually compatible with fat until proven otherwise but the Figure 4 are compatible with edema rather than muscular atrophy.

The observed venous congestion in areas distant from the interventional area both in patients surgically treated with opening of the extra-peritoneal space and in those without pelvic involvement, further confirms an alteration of pelvic structures following pelvic surgery.

MRs, also, identified other common features of lymphedema: accumulation of liquid in adipose tissue or lipedema. The estimate of body fat indicate an average BMI of 29.9 (so called overweight), since reduction of adipose tissue, where lymph nodes are predominantly concentrated, might contribute to the loss of pelvic structural continuity. Moreover, the specific structure of pelvic lymphatics must be considered, since it is ubiquitously and homogenously distributed as a thick net and conveys a three-dimensional appearance of volume, unlike the generally single long dimension that characterizes the upper or lower limb lymphatics. Surgery leads not only to the limitation of volume, but also to the involvement of all pelvic structures.

To date, lymphedema is frequently undiagnosed even in teaching centres, and it seems likely that many surgical interventions have not been adequately studied with respect to lymphatic damage and their consequences[23]. Although it could be argued that such observations are not essential when colorectal surgery is only limited to an internal pelvic space, and that any radiological image is only one indicator of type of surgical intervention, we detected signs of venous congestion in all pelvic areas, demonstrating that each surgical procedure implicates involvement of the entire pelvic structure. Thus, it is not the type of surgical intervention that creates favourable conditions for lymphedema, but rather the specific location of the pelvic floor where surgery occurs. The pelvis is a dynamic functional unit endowed with an elastic memory continually responding to changes of: body weight, intra-abdominal pressure due to increased loads caused by chronic conditions, and by the natural events of pregnancy and delivery. Elastic memory of the pelvis contributes in inhibiting the onset of lymphedema. However, surgical disruption of this functional unit, in particular impairment of the pelvic memory capability is exceeded can lead to hides lymphedema. Overall this can be the key factor in explaining pelvic dysfunction. Clinical evidence obtained by MR indicates that lymphatic vessels play a significant role in surgeries that involve perineum and the pelvic floor[24,25]. This preliminary report could answer the question how does pelvic lymphedema occurs?

## Conclusions

This report is limited to radiologic phenomena's after rectal surgery, and the clinical impact of

these signs (clinical aspects such as patients symptoms, quality of life or pelvic organ function), remains unclear. During surgery the primary cause responsible for the damage should be detected otherwise if, not promptly treated, it can result in a chronic disease. There are not described and it is not analyzed if the lymphedema detected after lower rectum surgery does has any consequences for patients health. However a better understanding of pelvic lymphedema could be the key to improving therapeutic strategies, including the routine use of biofeedback re-education of the pelvic floor, for functional abnormalities after pelvic surgery[26].

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### Disclosure of Interest

None.

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