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# Direct MRI Fistulography with Hydrogen Peroxide in Patients with Recurrent Perianal Fistulas: A New Proposal of Extended Diagnostics

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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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**Background:** Perianal fistulas are malformations of the anorectal area. Accurate preoperative assessment of perianal fistula tract is a main assumption in diagnosis of the disease, affecting the operation efficiency. The aim of the study was to present our experience in application of a new diagnostic protocol based on the magnetic resonance imaging (MRI) examination using a mixture of hydrogen peroxide (HP) and gadolinium as a direct contrast medium in evaluation of recurrent fistulas tract. The method is referred to as HPMRI.

**Material/Methods:** The study group consisted of 12 subjects operated on from 2011. Direct HPMRI fistulography was performed in all subjects before the operation. All types of fistulas were precisely evaluated by HPMRI examination.

**Results:** Intraoperative state confirmed complete course of fistulas in 11 cases. In 1 case, an internal opening was not found.

**Conclusions:** We suggest that this new method of direct HPMRI fistulography may improve visualization of the tracts of recurrent fistulas and improve efficacy of surgical procedures.

**MeSH Keywords:** Fistula • Magnetic Resonance Imaging • Perianal Glands

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## Background

*Fistula in ano* is a chronic infection of perianal tissues, which is usually a consequence of an abscess. Surgery is the only efficient therapeutic option. A fistula is burdensome for the patient, and may also constitute a serious therapeutic problem for the surgeon due to significant difficulties in determining the course of the fistula and its ramifications in relation to the anal sphincter and position of the internal opening.

Patients with recurrence of the disease constitute a significant problem. In that case, the difficult decision on method of therapy should be made following careful consideration of medical history, physical examination, and diagnostic imaging, expecting a non-typical course of the fistula. Erroneous decisions may result in recurrence of the disease or damage to the anal sphincter and fecal incontinence. Diagnostic tests are very helpful in precise determination of the scope of surgery. Accurate pre-surgical determination of the course of the perianal fistula canal is the basic purpose of diagnostics, and largely determines efficiency of the surgery. Fistula imaging using various magnetic resonance imaging (MRI) protocols has currently become the criterion diagnostic standard.

The aim of the study was to present our experience and suggest of a novel form of direct MRI fistulography with a mixture of 3% hydrogen peroxide (HP) and a paramagnetic agent as contrast for imaging and evaluation of recurrent perianal fistulas.

## Material and Methods

Twelve patients were enrolled into the study: 8 males, mean age 45.25 years (range 23–59), and 4 females, mean age 49.25 (range 39–58 years). All subjects underwent physical examination and imaging diagnostics, including: transrectal ultrasonography and direct MRI fistulography with a mixture of 3% hydrogen peroxide (HP) and paramagnetic agent based on the rare earth element gadolinium (Gd) as a contrast medium. For the study, the latter method was referred to as HPMRI. The study group included patients with recurrent fistula; patients with no patent external orifice were excluded. Two subjects from the study group were operated on twice and 1 was operated on 4 times. Evaluation of the main fistula canal was based on the Parks et al. classification [1]. Physical examination, instead of visual inspection, palpation of the anal area, and *per rectum* examination also included rectoscopy. HP was administered to the external orifice during the rectoscopy and a probe was introduced carefully. The probe was advanced towards the internal opening with palpation of its area. Following physical examination, transrectal ultrasonography was performed. The study radiologist was aware of results of previous examinations. Then, HPMRI fistulography was performed. The radiologist reading the MRI also was aware of results of all previous examinations. Each patient was operated on by the same surgeon (the most experienced one) who knew all examination results and additionally consulted directly the radiologist who read the MRI. HP and/or methylene blue dye was administered into the fistula during the surgery. Results of all examinations were compared to the actual state revealed during the surgery. That state was recognized as a reference and was the final one.

### HPMRI fistulography

Based on our experience in direct MRI fistulography with paramagnetic contrast medium solution (Gadovist, BayerShering Pharma) [2], we decided to extend the diagnostic abilities of the method by addition of HP instead of normal saline to the mixture. Concentration of contrast medium solution administered into the fistula lumen was determined empirically. For that purpose, 1 $cm^3$ of HP was introduced to 2-$cm^3$ plastic tubes, subsequently adding 1, 2, 4, 8, 16, or 32 drops of the paramagnetic contrast medium from a syringe with a 7-0 needle. No reaction between the 2 liquids was observed following addition. Tubes were placed in animal muscular tissue (porcine nape). Two drops of the contrasting medium added by a 7-0 needle to 1 $cm^3$ HP was found to be the most adequate. The obtained solution was then injected directly into animal muscular tissue with previously diathermy-formed canals. The MRI image of the muscular tissue with previously formed canals appeared as a clear "double-barrel" with hyperintensive canal walls and hypointensive lumen of that artificial fistula (Figures 1 and 2).

Abundant foaming and outflow of the contrast medium was observed following contact of the solution with the tissue.

The result of the examination of muscular specimens may offer better visualization of the internal opening of the fistula, and for improved tracing of the course of the fistula itself in MRI *in vivo*. That encouraged us to apply this new form of direct MRI fistulography in clinical practice.

HPMRI fistulography has been used for diagnostics of recurrent fistulas since 2011. Directly before the examination, a solution of contrast medium in HP was prepared *ex tempore* in proportion of 2 drops of Gadovist per 1 $cm^3$ of HP. The solution was administered into the fistula through its external opening, using a winged needle without a guide, in volume of a few $cm^3$. Then, the external opening was closed with a gauze swab and plaster. The GE SIGNA LX HS equipment with induced magnetic field of 1.5 Tesla was used for examination, with a dedicated 8-channel superficial coil placed at the level of iliac joints, using spin echo sequence (SE – spin echo, TSE – turbo spin echo) and obtaining T1- and T2-weighted images





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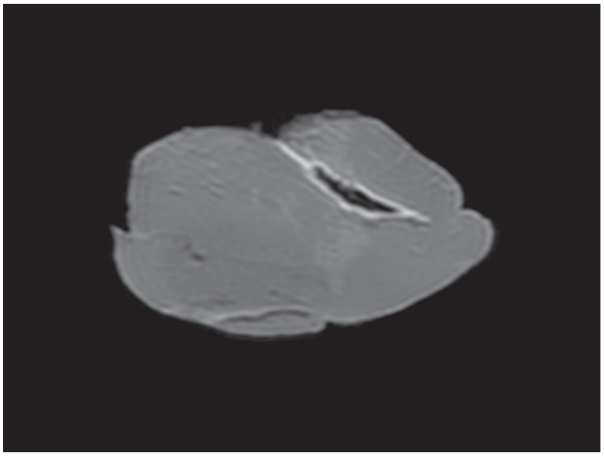

**Figure 1.** Direct HPMRI fistulography. T1 weighted image with fat saturation. Animal muscular tissue specimen. Lumen of diathermy-formed canals filed with mixture of HP and gadolinium (Gadovist) – "double-barrel effect".

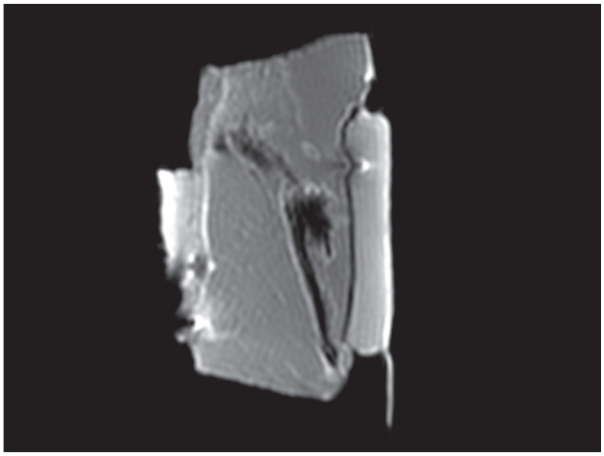

**Figure 2.** Direct HPMRI fistulography. T1 weighted image with fat saturation. Animal muscular tissue specimen. Lumen of diathermy-formed canals filed with mixture of HP and gadolinium (Gadovist) –"double-barrel effect".

**Table 1.** Results of evaluation of recurrent perianal fistulas in 12 patients.

| | Physical examination | Conventional ultrasound | MRHPI fistulography | Surgery |
|---|---|---|---|---|
| Primary tract (acc. to Parks) | | | | |
| Inter | 3 | 3 | 4 | 4 |
| Trans | 1 | 4 | 6 | 6 |
| Extra | – | – | 1* | 1 |
| Supra | – | 1 | 1 | 1 |
| Incorrect or unclassified | 8 | 4 | – | – |
| Internal openings | 4 | 4 | 11** | 11** |
| Additional lesions | – | 2 inter-sphincter cisterns | 1 anorectal abscess, 4 inter-sphincter cisterns and 1 supralevator cistern | 1 anorectal abscess, 3 inter-sphincter cisterns |

* Additional canal not confirmed by surgery; ** one opening, above the anal pectin, one internally blind fistula.

with saturation of fat tissue in axial (Ax), coronal (Cor), and sagittal (Sag) planes. Slice thickness was 4 mm, slice spacing was 1 mm, field of view (FOV) was 30 and 20, and NEX values were 4 or 3. Echo and repetition times for individual sequences were: T2 (TE/TR: 85/3000-4100) and T1 (TE/TR: 16/525-700).

All subjects provided written informed consent for the study.

## Results

Table 1 shows the number of correct determinations of the course of fistulas in physical examination, transrectal ultrasonography, and HPMRI fistulography in comparison to surgery as a reference state. Two horseshoe fistulas were recognized correctly in HPMRI fistulography.

## Discussion

Perianal fistulas are a heterogenous group of lesions of the distal section of the gastrointestinal tract and perineal area, referred to as anorectal malformations [3–6]. They are granulation-filled canals surrounded by hard fibrous tissue. Most of them are of adenoid origin, are cryptogenic, and have an elliptical course starting close to the anus, and having an internal opening in the rectal canal at the level of the crypts. The main role in pathophysiology of fistula formation is played by





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localization and quantity of perianal glands characteristic for that region, and direction of infection spreading along anatomical planes [7,8]. The Parks classification is based on the course of the fistula canal relative to the external sphincter, and divides perianal fistulas into 4 basic types: intersphincteric, transsphincteric, suprasphincteric, and extrasphincteric. Superficial fistulas form a separate group [1,3,6,7,9]. Other subtypes of fistulas encountered in the literature (simple, complex, multiple, high, and recurrent) are associated with their course, presence of additional canals and openings, and previous therapy. These factors determine the therapy of fistulas. In this paper, in addition to the Parks classification, we use the term "recurrent fistula", defined as a fistula formed following a previous, unsuccessful surgery. Fistulas that have no internal opening are internally blind. Sometimes, following penetration of the external sphincter muscle with the exit point in the posterior or middle gland, the purulent process penetrates soft tissues further, finding its circuitous way to the retroanal space, which that results in a horseshoe fistula.

A small number of fistulas present a complex, ramified course with a canal reaching over the puborectal muscle or cisterns filled with pus. More commonly, the internal opening of a fistula is narrowed, small, or even periodically closed. If that internal opening is not removed along with the gland localized between sphincters, if any additional canals or cisterns are not found and correctly drained or removed, the chance of recurrence is high. Difficulties encountered at evaluation of non-typical course of the recurrent fistula's canal may lead to omission or blind search during the surgery, and these unsuccessful attempts may result in formation of a false canal and opening, and consequently, unnecessary extension of the surgical field or incomplete excision of the fistula. "Blind" surgery may lead to omission of foci of pathological granulation – inflammatory foci. Excessively aggressive surgical procedures may lead to damage of sphincters and fecal incontinence, and excessively conservative procedures may lead to recurrence.

Therefore, the commonly unsuccessful surgical therapy of fistulas is associated with insufficient determination of their course and failure to locate all ramifications and internal openings. Moreover, difficult anatomic conditions limit aggressive diagnosis and therapy, both before and during the surgery, in the face of concerns about sphincter damage.

The percentage of compliance in determining the main fistula canal course with presurgical diagnostics compared to the course determined during the surgery varies, depending on the examination method, from 48% to 61% for physical examination, up to 80% for transrectal ultrasound, and to over 90% for MRI [7,9–12]. Each of those methods is associated with some benefits and limitations. Combined in cases of diagnostic uncertainties, they give very good results.

Endoanal ultrasonography (EAUS) is currently a broadly applied, non-invasive method for imaging of perianal fistulas, accompanied by increasingly popular and precise ultrasonography with application of contrasting medium HP (HPUS) [13–15]. However, in many cases EAUS and HPUS do not detect highly localized (suprasphincteric), subdermal lesions, those of horseshoe type, or with smaller additional branches. According to numerous authors, these methods should be used only for orientation, determination of post-surgical sphincter condition, or before minor procedures such as incision or drainage [7,8,16–18]. MRI is the method that, according to most authors, offers the highest sensitivity and specificity in diagnostics of fistulas, ramifications, internal openings, and abscesses compared to the clinical and ultrasound examination [16,18–21]. The high diagnostic efficacy of MRI in cases of recurrent fistulas demonstrated by Buchanan et al. [21] allows a clear efficacy improvement of therapy of those difficult forms of fistulas, reducing the ratio of post-surgical recurrences by as much as 75%.

MRI does not require any previous preparation and is well tolerated. Principal advantages of the method are high spatial resolution of the image, possibility of multiplanar imaging, and unlimited inter-procedural modification of the examination [3–5]. Due to a perfect tissue differentiation, all muscles of the rectum and pelvis are visible, particularly the levator ani muscle, as well as surrounding adipose tissue constituting a background [3–5]. Currently there is no single, universal, and commonly used protocol of MRI in case of suspected perianal fistula. The examination may employ endoanal and endorectal coils, offering a broader range, or superficial coils (pelvic, torso type) [22–25]. Examinations performed using endorectal coils have the highest spatial resolution. However, the technically limited scope of the examination significantly reduces usefulness of the method in diagnostics of highly localized and complex fistulas. The examination is also time-consuming and poorly tolerated by patients.

Another proposal is MRI fistulography with intra-fistular administration of paramagnetic contrasting medium (*direct MRI fistulography*) [2] or classic MRI with intravenous administration of contrasting medium (*indirect MRI fistulography*) [19]. Both methods use superficial, multi-channel coils that, considering field inductivity of modern MRI scanners (most commonly 1.5T), produce images of quality comparable to those from endorectal coils.

The efficacy of commonly used surgical methods depends on numerous factors: failure to locate the internal opening of the fistula, presence of additional canals invisible in examinations, erroneous evaluation of course of the fistula, presence of a horseshoe-shaped fistula, and premature wound closure following fistulotomy [17,26]. Maier et al. [16] demonstrated statistically higher efficiency in detection of perianal fistulas and abscesses with MRI (sensitivity 84%) compared to EAUS (sensitivity 60%) in a group of 39 patients. MRI gave false-positive results





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**Figure 3.** Indirect MR fistulography, axial plane, T1 weighted image with fat saturation. Complex perianal fistula with external opening on the right. Strongly enhanced inflammated fistulas walls after intravenous contrast administration.

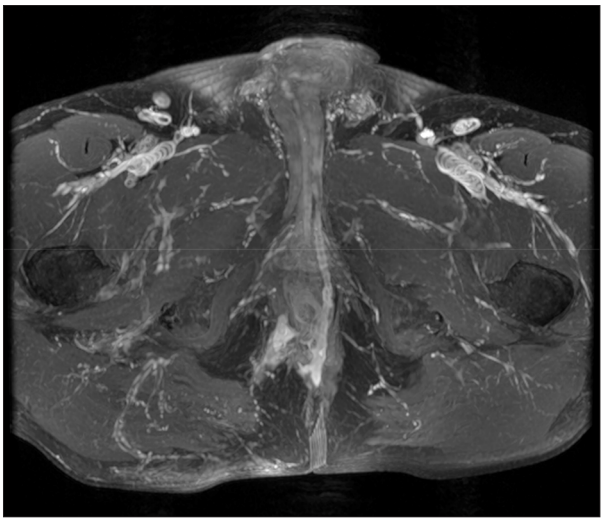

**Figure 4.** Indirect MR fistulography, axial plane, T1 weighted image with fat saturation. Maximum Intensity Projection (MIP). Complex, horseshoe perianal fistula. Strongly enhanced inflamed fistulas walls after intravenous contrast administration. Number of perianal vascular plexuses.

in 6 patients (15%) and EAUS in 10 patients (26%). Beets-Tan et al. [27] evaluated usability of the method, comparing results of MRI in patients before the surgery and the intra-surgical presentation. They demonstrated 100% and 86% sensitivity and specificity, respectively, for examination for detection of fistula canals; 100% and 100%, respectively, for evaluation of horseshoe-shaped fistula; and 96% and 90%, respectively, for detection of internal openings. Buchanan et al. [28] demonstrated that MRI increases the rate of correct diagnoses by 10% compared

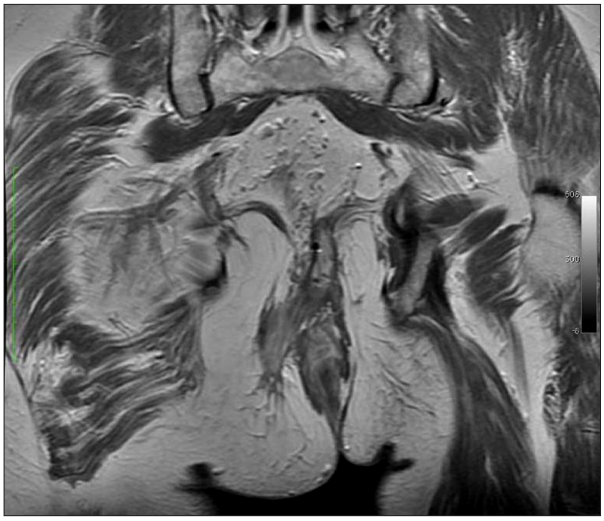

**Figure 5.** Direct MRI fistulography, coronal plane, T1 weighted image. Horseshoe fistula on the right. Hiperintense fistula canal filed with mixture of gadolinium and saline.

to EAUS, and that the ratio of recurrence following surgical interventions based on MRI diagnostics was 3 times lower.

The MRI method allows sufficient visualization of fistula canals and localization of pus cisterns, and allows much more precise evaluation of surrounding soft tissues compared to EAUS. Filling the lumen of a fistula only with normal saline improves its visualization in liquid-enhancing sequences (T2-weighted or inversion images). It seems that additional administration of HP during direct MRI fistulography allows better penetration of the solution into the internal opening and improves visualization of the fistula, additionally increasing sensitivity of the MRI method.

Intravenous administration of contrasting medium in MRI examination (*indirect MR fistulography*) allows visualization of inflamed fistula walls. These are intensively enhanced and more visible [18,19,29,30]. Sometimes vascular plexuses located in the same area pose some serious interpretation problems. Contrast-enhanced, they imitate pathological fistula canals. This may reduce specificity of indirect MR fistulography (Figures 3 and 4).

We suggest that simultaneous indirect and direct MRI fistulography with administration of contrasting medium and HP may bring greater diagnostic benefits than using these 2 examinations separately.

The application of HPMRI for diagnostics of some gunshot wounds may be possible, but we lack sufficient experience in that field and cannot offer any clear recommendations.

Fifty-seven recurrent fistulas were surgically treated in our center from 2006 to 2012. The number was 35.2% of all fistula surgeries. Initially, direct MRI fistulography was used for





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**Figure 6.** Direct HPMRI fistulography, axial plane, T1 weighted image with fat saturation. Extrasphincteric perianal fistula on the left side. Lumen filed with mixture of HP and gadolinium (Gadovist) – "double-barrel effect".

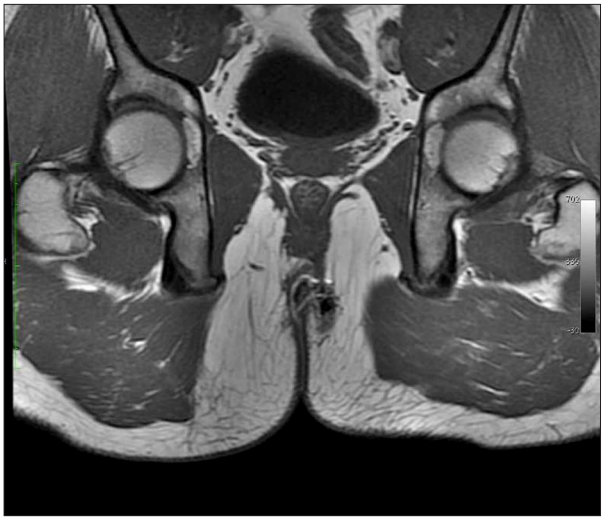

**Figure 7.** Direct HPMRI fistulography, coronal plane, T1 weighted image. Small horseshoe perianal fistula. Lumen filed with mixture of HP and gadolinium (Gadovist) – "double-barrel effect".

diagnostics, with a mixture of paramagnetic agent (Gadovist) and normal saline as a contrasting medium [2]. In obtained images, lumen of the fistula filled with the solution demonstrated strong enhancement in sequences sensitive to contrasting medium (T1-weighted images) (Figure 5).

HPMRI has been used since 2011. The procedure of the examination has not changed, but short-term pain and spreading sensation was reported by 3 patients during contrast administration into the external opening of the fistula. Slower contrast administration allowed reduction of those minor complaints. We stress the much easier evaluation of the fistula canal, due to the "double-barrel effect" (Figures 6 and 7).

We speculate that the effect may be a result of 2 potential phenomena. First, due to its oxidative and disinfecting properties, hydrogen peroxide may provide mechanical and chemical purification of fistula canal tissue, changing their texture, which allows better adherence of contrast medium to internal fistula walls. Second, catalyzed by inflamed tissue, blood, bacterial enzymes decomposition of HP into water and oxygen *in statu nascendi* may allow formation of additional complexes of Gd with ions from altered tissues. Precise understanding of that phenomenon requires further experiments.

In our study, types of fistulas were precisely evaluated in all patients based on HPMRI fistulographic examinations that allowed appropriate preparation of patients and of the whole surgical team for the surgery. In 11 patients, a complete course of fistula was determined, revealing additional ramifications, and cisterns of pus and granulation. An internal opening was not found in 1 case and the orifice was also not found during the surgery. In that case, the operating surgeon, based on his own experience, decided that it was a case of internally blind fistula. In 1 case, 2 additional branches of the fistula were not found. Supralevator abscess was not found as well, just cisterns of granulation.

## Conclusions

Pre-surgical precise localization of the course of a perianal fistula, along with its external and internal opening, is a basis of diagnostics of recurrent perianal fistulas, being a condition of high surgical efficacy.

Based on our own experience and the available literature, we believe that direct MRI fistulography with administration of the paramagnetic contrast medium, gadolinium, and 3% solution of hydrogen peroxide may additionally improve visualization of a recurrent fistula. HPMRI fistulography appears to have high diagnostic value in determining the course of the fistula canal. The procedure reveals the relation between the fistula and sphincters, and identifies its internal opening and ramifications. It also allows precise planning of the surgical procedure, and therefore improves its efficacy.

We believe that HPMRI fistulography should be widely used, gradually improved, and that new applications of the method should be found.

### Conflict of interests

The authors declare that there is no conflict of interest regarding the publication of this article.





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