

# Value of MR imaging in diagnosis and follow-up of perianal fistula after fibrin sealant

*Manal F El Tohamy,<sup>a</sup> MD; Doaa Omar Refaat,<sup>b</sup> MD*

*a) Department of Radiology, Zagazig University, Egypt.*

*b) Department of General Surgery, Zagazig University, Egypt.*

## Abstract

*Fibrin glue has recently been shown to be a successful modality for treatment of complex perianal fistulas and is associated with a higher degree of patient satisfaction. Fistula healing after fibrin glue application can only be determined by adequate follow-up, with consideration of underlying tract activity not just skin healing which can be achieved by MR imaging. This study was designed to evaluate the role of MR imaging in patient selection and prediction of outcome of fibrin sealant treatment in patients with complex perianal fistulas. Twenty-four patients underwent fibrin glue after fistula tract preparation and followed up for a median of 16 months. Clinical and MRI assessment were performed to patients who had early signs of skin healing. Based on their preoperative MRI appearances, 17 patients (70.8%) had transsphincteric fistula, 5 (20.8%) had suprasphincteric fistula and 2 (8.4%) had extrasphincteric fistula. Twenty cases (83.3%) showed skin healing at a median of six (range, 2-15) weeks, 14 cases out of them remained healed till the end of follow up period (range 9-26 months) while 10 cases had relapses and fistula recurrence. The success rate was 58.3% while recurrence was reported in 41.7%. In conclusion, fibrin sealant injection is a safe and useful treatment in the management of complex perianal fistula and precludes the need for more extensive surgery. MR imaging can accurately predate the clinical assessment in prediction of the outcome at an earlier stage. More than one half of the patients can actually be cured with fibrin glue when considering combined clinical and radiological evidence.*

## Introduction:

Surgical management of complex perianal fistulas is challenging and may be associated with the risk of sphincteric injury. Fibrin sealant has been used in many surgical conditions. Several successful trials of using fibrin sealant in the treatment of fistula in ano have been performed.<sup>1,2</sup> By using fibrin sealant in treating complex perianal fistula, patients can avoid the risks of staged seton procedure and the morbidity associated with operative treatment such as fecal incontinence, wound pain and discomfort associated with post-operative wound dressings.<sup>3</sup> Fibrin sealant is a tissue sealant that uses the activation of thrombin to form a fibrin clot, which mechanically seals the fistula tract. The clot undergoes gradual fibrinolysis while promoting tissue healing processes to permanently obliterate the fistula tract. Over the past few years, imaging, notably MR, has revolutionized the treatment of patients

with fistula in ano.<sup>4,5</sup> Recently, MR imaging has emerged as a promising tool for preoperative classification of fistula in ano. The ability of MR imaging to help not only accurately reveal the location and extent of the disease, including a clinically undetected fistula or abscess but also influence the subsequent surgery and patient outcome.<sup>6</sup>

## Aim of the work:

This study was designed to evaluate the role of MR imaging in patient selection and prediction of outcome of fibrin sealant treatment in patients with complex perianal fistulas.

## Patients and methods:

Twenty-four patients participated in our study suffering from complex perianal fistula. They were 19 males and 5 females, (their ages 32-55 years; mean age 43±9.3 years). All

patients were preoperatively examined by a surgeon for eligibility to participate in this study followed by MR imaging of the perineum before fibrin sealant injection in order to delineate the fistula tract, exclude an abscess or other underlying pathology. Post-operative MR imaging was arranged during the follow-up period to monitor the activity of the fistula. Determination for inclusion was undertaken by clinical examination and preoperative MR imaging. The study included patients with complex perianal fistula of cryptogenic origin encompassing at least one third of the external anal sphincter muscle by preoperative MR imaging. The exclusion criteria were patients with clinical signs of persisting sepsis, side branches according to MR imaging, immunodeficiency, known hypersensitivity to fibrin glue, those aged less than 18 years, and females who were currently pregnant or were considering becoming pregnant. Patients were followed up for a median period of 16 (range, 9-26 months). Three patients had previous surgical attempts.

#### **MR imaging technique and interpretation:**

MR technique was performed for all patients using (GE Signa Contour, 0.5 T machine) with body coil. Patients were scanned in the supine position. The long axis of the anal canal was identified with a midline sagittal localizing scan. The transverse sections were taken at a right angle to the anal canal while the coronal sections were parallel to the canal. The subcutaneous tissue overlying the gluteus region was properly involved since perianal complications commonly extend to the subcutaneous tissue. No bowel preparation or special equipment (no catheterization of the anal canal or the fistula) was required for the examination. Each examination included T1-weighted fast spin echo images (600/15 TR/TE) in the coronal plane. STIR imaging (1800/20/150 T1, or inversion time) in the coronal plane. T2-weighted axial spin echo images (2000/30, 60 TE) sequences. Post-operative dynamic contrast enhanced MRI was performed to all patients with skin healing during the follow up period and included T1 weighted contiguous coronal slices. The scans were taken immediately before and 10, 30 and 50 seconds after intravenous gadolinium

injection. Fistulas were defined according to Parks et al.<sup>7</sup> classification. Fistulous tracts were differentiated from abscesses by using the criteria of Laniado et al.<sup>8</sup> in which fistulas were defined as being fluid-filled tubular structures with a diameter smaller than 10 mm and abscesses were larger than 10 mm. Air pockets within the fluid collection also suggested the presence of abscess.

#### **Surgical procedure:**

The surgeon explained the study objectives, risks and benefits associated with the procedure to all patients. Informed consent was obtained from every patient prior to the study. On the evening before surgery, all patients underwent mechanical bowel cleansing enema. Parental antibiotics using 1 gm of cefotaxime and 500 mg of metronidazole were administered before induction of anesthesia. The procedure took place as one day case surgery under general (n=16) or spinal (n=8) anesthesia with the patient placed in the lithotomy position. Clinical examination and proctosigmoidoscopy were performed. Both internal and external openings were identified using conventional fistula probes. Once the fistula had been delineated, the primary tract was thoroughly curetted with a spoon to remove all granulation tissue. If the tract was narrow, curettage was undertaken with a thin gauze strip or braided suture material. Fistulas were cleansed with hydrogen peroxide 1.5% and normal saline 0.9% mixed in equal parts. Gauze was packed in the rectum of the patient before injection to prevent spillage of fibrin sealant into the rectum or anal canal. A commercially made fibrin sealant was used. Before application, the fibrin sealant was prepared and kept at room temperature, as recommended by the manufacture; FIBINGLURAAS-Fibrin sealant (Human), Shanghai RAAS blood products Co. Ltd.). Two components were prepared (component 1: fibrinogen concentrate, human plasma protein fraction with factor XIII activity and aprotinin; component 2: thrombin and calcium chloride solution). They were then siphoned into two syringes and connected to a dual chamber applicator. The dual chamber applicator syringe was put inside the fistula tract through the external opening and fibrin sealant was injected until the whole tract was

filled with sealant. The patient was then instructed to have a half-hour period of rest to avoid back flow of fibrin sealant and allow fixation of the fibrin plug. After that, the gauze pack was removed and a one week course of oral antibiotics was prescribed (cefuroxime 250 mg t.d and mitronidazol 500 mg t.d.s). Median operative time was 20 (range, 14-26) minutes, with a median of 2.5 (range 0.8-6) ml of glue required to ensure tract filling.

#### Follow-up:

All patients were followed up as surgical outpatient for a median of 16 (range 9-26) months with attention to clinical evidence of healing and signs of recurrence. Recurrence was defined as discharge, pain, and visualization or palpation of either internal or external fistulous opening. Healing was defined as absence of these symptoms. Patients with fistula recurrence were offered additional injection of fibrin sealant, accepted only by one patient and has also failed. If healing was detected at the initial outpatient assessment, postoperative MRI (STIR and dynamic contrast-enhanced sequences) was performed at a median of six (range, 2-15) weeks after surgery to determine whether an underlying fistula remained in those patients with skin healing. Tracts associated with increased signal intensity on dynamic contrast enhanced MRI study were defined as active fistulas and predicted recurrence, whereas tracts with unchanged signal intensity were classified as inactive, representing healing. No patients defaulted follow up at the end of the study period. Three patients reported adverse events in the form of minor pain (n=2) and pruritus (n=1) which were mild and self-limiting.

#### Statistical analysis:

MRI findings were correlated with the surgical results and patient outcome. The success rate of fibrin glue treatment was determined by the proportion of patients who remained healed at the end of the study period. The accuracy, sensitivity, specificity, positive predictive and negative predictive values of clinical and MRI assessment in predicting outcome were calculated.

#### Results:

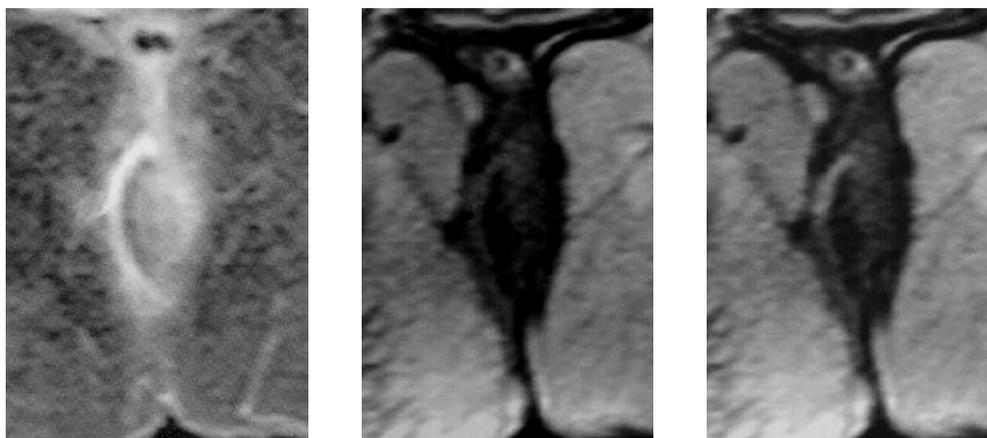
A total of twenty-four patients were enrolled in this study suffering from complex perianal fistula. They were 19 males and 5 females, (their ages 32-55 years; mean age 43±9.3 years). Based on their preoperative MRI appearances, 17 patients (70.8%) had transsphincteric fistula, 5 (20.8%) had suprasphincteric fistula and 2 (8.4%) had extrasphincteric fistula. Three patients (12.5%) had previous surgical attempts (Two were transsphincteric and one was suprasphincteric) **Table(1)**. After fibrin glue instillation, 20 cases (83.3%) showed skin healing at a median of six (range, 2-15) weeks, 14 cases out of them remained healed till the end of follow up period with a success rate of (58.3%) while 10 cases (41.7%) had relapses and fistula recurrence. Clinical and MRI assessment were performed to patients who had early signs of skin healing. The clinical evaluation failed to predict recurrence in four cases in which the openings healed temporarily while combined STIR and dynamic contrast-enhanced MR imaging predicted the outcome more effectively, except in one patient in which a tract was visualized on STIR sequence and the fistula did not subsequently recur **Table(2)**.

*Table (1): Clinical and MRI outcome of 24 patients with complex perianal fistula.*

| Parameter               | Success    | Failure   |
|-------------------------|------------|-----------|
| No. of patients         | 14         | 10        |
| Male/female             | 11/3       | 8/2       |
| Mean age (range, years) | 41 (32-51) | 43(37-55) |
| Type of fistula         |            |           |
| Transsphincteric (n=17) | 10         | 7         |
| Suprasphincteric (n=5)  | 3          | 2         |
| Extrasphincteric (n=2)  | 1          | 1         |
| Previous surgery (n=3)  | 1          | 2         |
| Follow up period        |            |           |
| Mean (range,months)     | 19 (11-26) | 16 (9-23) |

*Table (2): Accuracy of clinical and MRI assessment in predicting the fistula recurrence.*

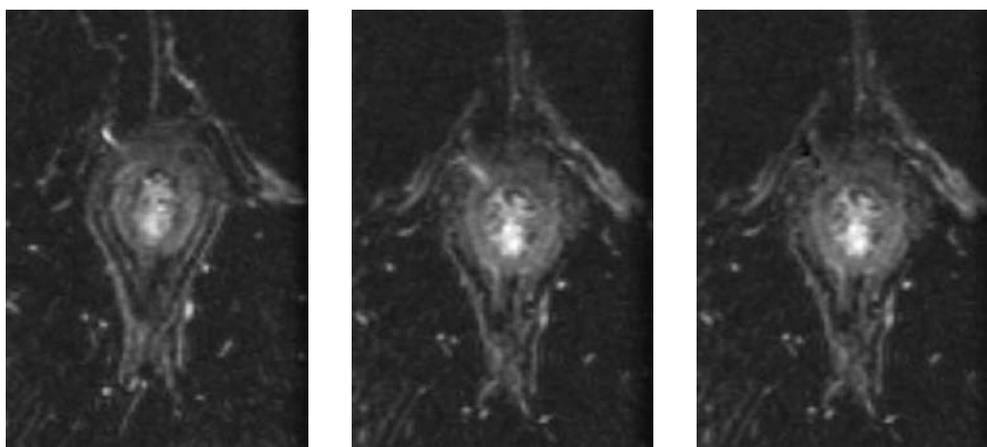
| Assessment           | Sensitivity | Specificity | Accuracy  | PPV       | NPV         |
|----------------------|-------------|-------------|-----------|-----------|-------------|
| Clinical examination | 33.3(2/6)   | 100(14/14)  | 80(16/20) | 100 (2/2) | 77.8(14/18) |
| MRI sequences        | 100 (6/6)   | 92.9(13/14) | 95(19/20) | 85.7(6/7) | 100 (13/13) |



*Figure (1): A case of suprasphincteric perianal fistula. Coronal short inversion time inversion recovery (STIR) sequence MR imaging showed high signal intensity fistula tract. T1 weighted images showed low intensity of the tract which increases after contrast enhancement suggesting recurrence.*



*Figure (2): A case of suprasphincteric fistula. Coronal STIR sequence MR imaging, two fistula tracts were detected in the ischioanal region. On the RT side, the fistula tract runs over the puborectalis muscle which persists after the fibrin glue treatment.*



*Figure (3): A case of transsphincteric perianal fistula. Axial fat suppression T2 weighted MR imaging showed the high intense fistula tract with mucosal opening at 11 o'clock which completely resolved several months after fibrin glue treatment.*

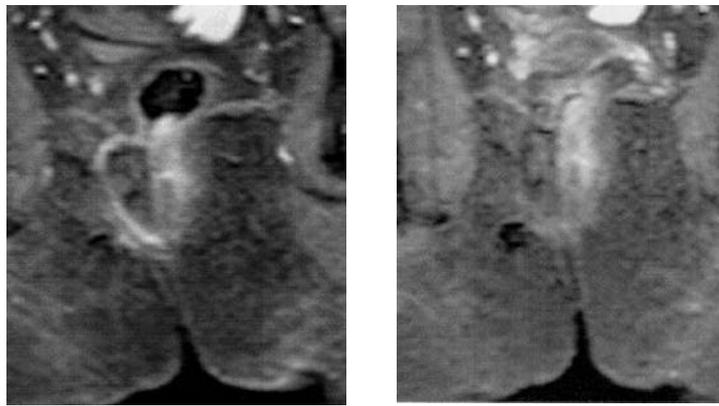


Figure (4): A case of transsphincteric perianal fistula. Coronal STIR sequence MR imaging showed high signal fistula tract which completely resolves after fibrin glue treatment.

### Discussion:

Fibrin glue has recently been shown to be more successful for complex fistulas than conventional treatment because it is simple to perform and obviates the need for inpatient stay, dressing changes, long period of convalescence, failure does not compromise further treatment options and sphincter function is preserved.<sup>9</sup> In the present study, 20 cases (83.3%) showed skin healing at a median of six (range, 2-15) weeks, 14 cases out of them remained healed till the end of follow up period (range 9-26 months) while 10 cases had relapses and fistula recurrence. The success rate was 58.3% while recurrence was reported in 41.7%. Our results suggested that fistulas may relapse after glue treatment despite initial apparent skin healing. The success rate reported in published studies range from 0% to 100%, these diverse results may be contributed to differences in patient selection, treatment protocols, and follow-up duration (10-14). Other investigators reported recurrence in 50% of patients within eight weeks of treatment despite proper tract preparation.<sup>15,16</sup> Maralcan et al.<sup>17</sup> revealed an overall initial success rate of 77.8% which reached to 83.3% after successful reapplication of fibrin glue in two patients. Johnson et al.<sup>5</sup> mentioned that most failures of fibrin glue patients occurred early in the follow-up and was thought to represent extrusion of glue shortly after surgery. Cintron and his colleagues<sup>18</sup> stated in their work that most treatment failures occurred within the first three months but late failures were seen as far as eleven months. As regard the adverse effects of fibrin sealant injection, in our study,

three patients reported adverse events in the form of minor pain (n=2) and pruritus (n=1) which were mild and self-limiting. Zmora et al.<sup>12</sup> reported many adverse effects in 47% of patients, the majority were mild and self limited such as minor pain, pruritus and perianal abscess which needed drainage whereas no adverse effects were reported by Hammond et al.<sup>10</sup> and Chan et al.<sup>3</sup>

Many studies assessing sphincter-preserving treatments for anal fistula have used skin healing as a predictor for fistula healing.<sup>4</sup> In this study, we use MRI as a non invasive tool to monitor fistula healing. Although only one case was classified as false positive on STIR sequence, combined STIR and dynamic contrast-enhanced MRI was superior to clinical assessment in predicting the outcome after fibrin glue application (for MRI: sensitivity, 100%, specificity, 92.9%; accuracy 95%; PPV, 85.7%; NPV, 100% versus sensitivity, 33.3%; specificity, 100%; accuracy, 80%; PPV, 100%; NPV, 77.8% for clinical examination). Buchanan et al.<sup>9</sup> mentioned that although all assessments in their study showed a high accuracy for determining recurrence, MRI could predict recurrence well in advance of clinical setting (accuracy of 100% versus 71%). Spencer and his co-workers<sup>19</sup> stated that MRI has an important role in the management of perianal fistulas. It shows the surgical anatomy, their complications and is a more accurate indicator of treatment prognosis than the findings of clinical examination. Moreover, Zmora et al.<sup>12</sup> suggested that pelvic MRI is a highly sensitive tool in delineating the fistula tract, may show postoperative patent fistula

tracts despite the absence of drainage through the fistula openings, potentially related to late clinical recurrence.

In conclusion, fibrin sealant injection is a safe and useful treatment in the management of complex perianal fistula and precludes the need for more extensive surgery. MR imaging is the most accurate method for determining the presence and course of anal fistulae. Also, MR imaging can accurately predate the clinical assessment and can predict the outcome in patients with skin healing. More than one half of the patients can actually be cured with fibrin glue when considering combined clinical and radiological evidence.

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