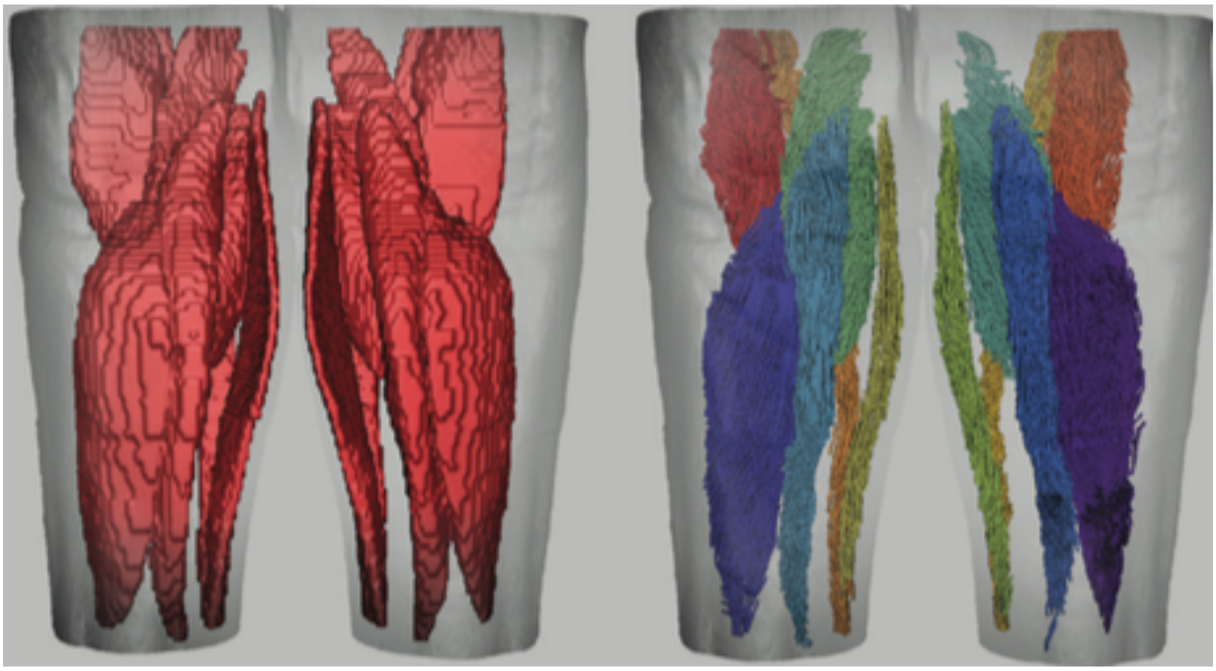

An innovative MRI technique for acute hamstring injuries

A feasibility study of micro-structural recovery at return to play

Title	**An innovative MRI technique for acute hamstring injuries** **A feasibility study of micro-structural recovery at return to play**
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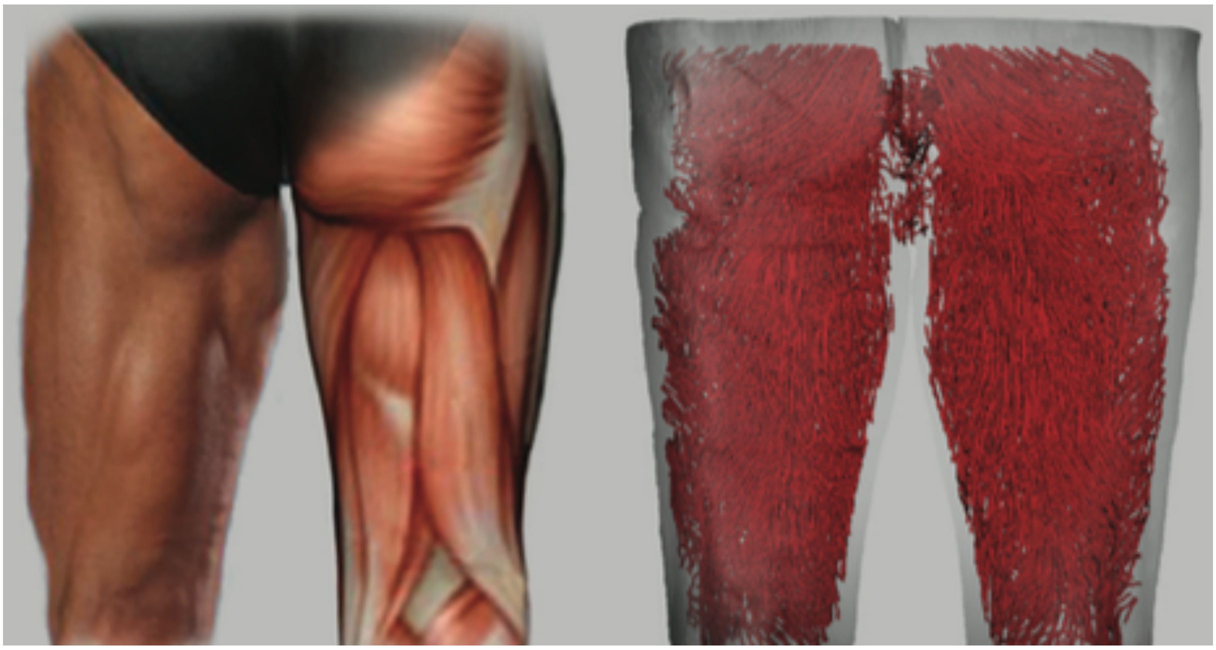

INTRODUCTION AND RATIONALE

The Hamstrings is a collective term for a group of muscles located at the posterior side of the upper leg. The Hamstring Muscle complex (HMC) consists of 3 components: the semitendinosus, semimembranosus, the long and short heads of the biceps femoris muscle[1]. Hamstring injuries are fairly frequent among athletes. These injuries usually occur during sprinting, high intensity running or sudden explosive movements such as jumping, twisting and turning[2]. Hamstring trauma is usually found in the biceps femoris muscle as it undergoes the most stretch in comparison to the other components of the HMC[2].
Hamstring injury is known for its high recurrence rate; 22-34% of athletes will have a re-injury within 1 year following rehabilitation[1,3]. Importantly, studies regarding potential prognostic markers for predicting the best time for "return to sports" after a hamstring injury are scarce.

Although the available literature concerning prognostic factors for acute hamstring injuries is scarce, there are some studies that defined some. Verrall et al.[4] found that MRI and clinical assessment were relative accurate prognostic factors for the convalescent period.
MRI appeared to be more useful in predicting the rehabilitation of moderate to severe cases whereas clinical assessment showed to be more accurate in lighter and MRI negative injuries. Furthermore, Verrall et al.[4] also observed that the likelihood of recurrence was increased by a factor 2.2 when the transverse size of the injury was greater than 55% of the muscle. Another supposed prognostic factor is the deficit in knee active range of motion (AROM) between both legs measured 48 hours following the injury. This was supposedly accurate in predicting the convalescent period.
Additional prognostic factors are described by Brooks et al.[5] (1) injury to the proximal free tendon would require a longer convalescent period, (2) the relative distance of the palpable location of maximum pain from the ischial tuberosity would be associated with the rehabilitation time needed (with proximity to the ischial tuberosity generally meaning a longer recovery period) and finally (3) the area of both the length and cross-section of the injury depicted by MRI would be an accurate prognostic marker.
Despite the fact that MRI has improved our knowledge about this frequent injury, there are three limitations identified:

- Prediction: There is a lack of evidence for any MRI categorical or continuous parameters for predicting the time to return to sports.
- Monitoring recovery : There is a lack of evidence for the value of MRI for monitoring recovery.
- **Decision making: There is a lack of evidence for the value of MRI for guiding the return to sports decision making process.**

This means that new and more accurate methods are needed in order for us to efficiently predict the convalescent period and readiness for RTP of an athlete after a hamstring injury.

A relatively new and potentially more sensitive technique for assessing muscle injury is Diffusion tensor imaging (DTI)[6]. DTI is a MRI-based technique which measures the self-diffusion of water influenced by intra and extracellular structures and therefore provides information of tissue microstructure[7]. Recent literature of skeletal muscle injuries showed DTI to be feasible in muscles. Froeling et al.[8] also showed that DTI has sensitivity for muscle changes beyond the capabilities of conventional imaging techniques. Although DTI seems promising, no long-term follow-up study has yet been performed which correlated findings with clinical tests.

In this project, we will advance our DT-MRI technology for monitoring recovery of micro-trauma at return to play. This will make DT-MRI clinical relevant for guidance of the return to play decision following sports-related muscle trauma.

2. Questions and hypothesis.

Our first hypothesis is that DT-MRI is a feasible technique for evaluating muscle fibre appearance at return to play. Our second hypothesis is that detailed monitoring of structural recovery through DT-MRI and fibre tracking techniques will support a robust return to play decision and potentially reduce the chance of repetitive injury.

Based on these hypotheses our 2 main research questions are:

1. Is DT-MRI a feasible technique for evaluating muscle fibres **at return to play (RTP)?**
2. Can DT-MRI accurately visualize muscle fibres **at return to play** through fibre tracking techniques?

Methods

STUDY DESIGN

This is a single centre, diagnostic observational study, football players will be included. The patients in this study consist of a prospective cohort of patient with acute hamstring injuries. The study started in September 2016 and was performed at the sports medicine and radiology departments of a university hospital.

STUDY POPULATION

Population (base)

Athletes (predominantly football) with a suspected hamstring injury were recruited. Athletes, physical therapists, team physicians, sport associations and clubs were informed about the study. Information about the study will be published on our website www.hamstringonderzoek.nl. Referring physicians and therapists were informed about the criteria for inclusion.

Inclusion criteria

Clinical diagnosis of an acute hamstring injury ≤ 7 days old, defined as:

- Anamnestic acute injury.
- Anamnestic pain in posterior thigh.
- Localised pain during palpation of hamstring muscle.
- Localised pain during passive straight leg raise.
- Increasing pain during isometric contraction.
- Age > 18 years old.

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

- Patient is not capable of doing an active exercise program.
- Patient does not have the intention to return to full sports activity.
- Cause of hamstring injury is an extrinsic trauma on the posterior thigh.
- There are contraindications for MRI: pacemaker, pregnancy, and claustrophobia.

- Re-injury ≤2 months after RTS after acute hamstring injury.
- Chronic hamstring injury >2 months; defined as recurrent pain or tenderness of the Hamstrings.
- Complete ruptures to the HMC will be excluded due to their different course of recovery. These patients will be referred to an orthopaedic surgeon for further treatment.
- Other concurrent injury inhibiting rehabilitation.

Study procedure

Patients were included at the AMC. During the first appointment the patient were physically examined by the investigator or a qualified member of the research team, which took approximately 15-30 minutes.
Experienced, registered sports medicine physicians with more than 10 years of clinical experience made the clinical diagnosis of the hamstring injury in medical care of athletes in sports where hamstring injuries are common (football, rugby, field hockey). The rehabilitation programme was supervised by a sport physiotherapist at the club or in the living area of the athlete. Subjects were cleared by the club medicals staff and/or treating physical therapist. Advise for clearance including successfully finished a physiotherapy programme and functional sport specific activities should be performed symptom free. After RTP clearance, athletes were advised to complete five days of team training before participating in partial match play and perform eccentric exercises as secondary prevention. At inclusion, informed consent was obtained from all patients.

If the patient met the criteria for inclusion he or she will be informed in more detail about the study procedure. At that moment the patient could ask questions about the study and decide to participate in the study. If the patient agrees to participate in the study, he/she can sign the informed consent form. Subsequently the patient will be scheduled for MRI, which will take approximately 45 minutes per MRI. The DTI (MRI) scans as well as the

questionnaires and the clinical tests will be performed at every appointment, coinciding with each other in order to better compare the findings. There will be 4 standard appointments and in the event of a relapse injury, 5 appointments.
For this study follow-up was at return to sports and, if indicated, at re-injury within 2 months of the index injury.

MRI

Following inclusion, the patient will underwent DTI (MRI) scans in order to assess the status of the injury.
The time points were:

- At inclusion. The scans will be within 7 days of the index injury, both scans on the same day in order to assess reproducibility.
- Just before/at return to play (**these will be analysed for this study**).
- Immediately after re-injury, only if there is a re-injury.

Both legs underwent imaging in order to compare the injured to the uninjured leg. The following MRI sequences shall be used: T1- and T2- weighted images, mDixon and DTI. Total imaging duration is 45 min. mDixon, T1- and T2- weighted images are components of the standard MRI protocol for hamstring injuries.

Self-reports

The athletes were required to fill in questionnaires in order to illustrate their perception of the injury. On these self-reports, the patient could specify the perceived restriction (it be sprinting or shooting) caused by the injury.

Clinical examination

Clinical examination was performed at every visit. Findings were scored accordingly on a standardized form. The function of the leg is tested and compared to the restrictions experienced by the patient. During clinical examination we will observe the extension of the knee. Furthermore the hamstring will be subjected to stretch, concentric and eccentric resistance in order to document pain, which would be expressed using VAS scores (Pain scale from 1 – 10).

Follow –up

The patients contacted the investigator as soon as possible in the event of a suspected re-injury. Patients were also contacted by phone every other month for a 2 month after the initial injury for follow up in order to obtain information about possible hamstring injuries (and we will continue up to one year). This is just in case the patient forgets to call.

In conclusion:

First visit: within 7 days: self-reports, clinical examination, 2 x MRI.

Second visit: +/- at return to play: self-reports, clinical examination, MRI.

Third visit: only In the event of a relapse injury (15-30% of patients): self-reports, clinical examination, MRI.

Follow Up by telephone: every other month for 1 year after the index injury.

TREATMENT OF SUBJECTS

There was no experimental treatment of the patients. All patients were advised to perform physical therapy with their physical therapist. (According to standard treatment)

Magnetic Resonance Imaging

In each subject MRI of the injury was performed twice: within seven days from injury and at RTP.

MRI protocol

One standardized protocol was used. To locate the area of the injury the entire hamstring of the injured limb was visualised by obtaining coronal and sagittal images from the ischial origin of the hamstring muscles to insertion on the fibula and the tibia. The thickness of the slices for all sequences was 5mm. MR images were obtained with a 3.0-T Philips MRI system with the use of an anterior body coil.

All MRIs are performed in a standardized manner. The patient lies supine for during a period of 45 min. Besides DTI, mDixon, T1 and T2 weighted images are used for normal healthcare purposes.

The subject was positioned head first in supine position.. The DTI acquisition was done in 12 gradient directions and 10 separate b-values ranging from 0 to 600 s/mm2 were obtained for IVIM modeling. The data was post-processed using DTITools for Wolfram Mathematica.

Re-injury

We recorded acute hamstring injuries that occurred within two months after RTP at the same site as re-injuries.[15]

Outcome – Fibre tracking was scheduled for evaluating muscle fibres **at return to play (RTP) and** accurately visualizing muscle fibres **at return to play** through fibre tracking techniques was evaluated. Mean Diffusivity (MD) and Fractional Anisotropy (FA) were evaluated at baseline and return to play.

Analysis

We planned performing all statistical analysis with SPSS software (version 20.0; SPSS, Chicago, Illinois), using descriptive statistics.

Results

From the start of the study till March 31st 2017, we included 27 athletes. Out of the 27, 2 athletes did not complete the RTP MRI assessments (lost to follow-up), 2 had complete avulsions (requiring surgery and no RTP MRI), 4 had a MRI and DTI negative injury and 4 were no at the stage of RTP MRI. Out of the 15 athletes available for analysis, there were 13 football players: premier League Eredivisie (N=3), First League (N=5), Second/third league (N=2), amateur league (N=2); (Table 2)

Table 2 Patient characteristics

Median age (min - max)	26.7 (19-34)
Gender Male / Female	15 / 0
Level of Football (only football players)	
- Premier League	3
- First League	5
- Second/third league	2
- Amateur league	3
- Others	2
Level of Sports (all athletes)	
- Professional	.10
- Competitive	5
- Recreational	0.

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For 8 out of the 15 athletes (13 footballers), the date of RTP was reached before our analysis at March 31st.

Our PhD has successfully finalised the internal training MRI program, which enables scanning during afterhours. More than 40% are now scanned post injury during the weekend and evenings. The responsible radiologist is 7*24 hours available and provides the report within 1 working day. The study has been announced among all professional football clubs, who can contact the investigators 7*24 hours, reflecting our elite-athlete clinical setting

The mean time between injury and presentation at the study centre was 5 days and between injury and MRI examination 5 days. The primary injury was to the long head of the biceps femoris muscle (n=12, 80 %), semimembranosus (n=2, 13%), semitendinosus (n=1, 7%) or the short head of the biceps femoris (n=0, 0%).

Conventional MRI analysis

At return to play conventional MRI showed hyperintesity in all players,

Except four players with a grade 0 injury on standard MRI imaging and DTI imaging.

DTI MRI analysis

The mean time for analysis of one DT-MRI data set was 25 hours, subdivided in 20 hours muscle segmentation (if only one muscle is affected, otherwise an additional 8 hours was required) and 5 hours data post processing. DTI analysis of 5 subjects showed that current post processing methods was faulty. We chose to perform whole muscle segmentation and separate dataset registration, as shown in Fig 1 and 2. Current consensus is that segmentation of the lesion and registering DTI datasets on each other is a much more accurate way of determining DTI parameter change in time.
Current analysis showed that fibre tracking techniques for evaluating muscle fibres **at return to play (RTP) is insufficient for** accurately evaluation.
New post processing and segmentation methods are warranted for optimisation of DTI MRI muscle injury techniques.

Re-injury

We recorded no re-injuries within two months after RTP.

Fig 1. Mean Diffusivity (MD) **of 5 processed DTI MRI data sets with segmentation of the complete muscle**

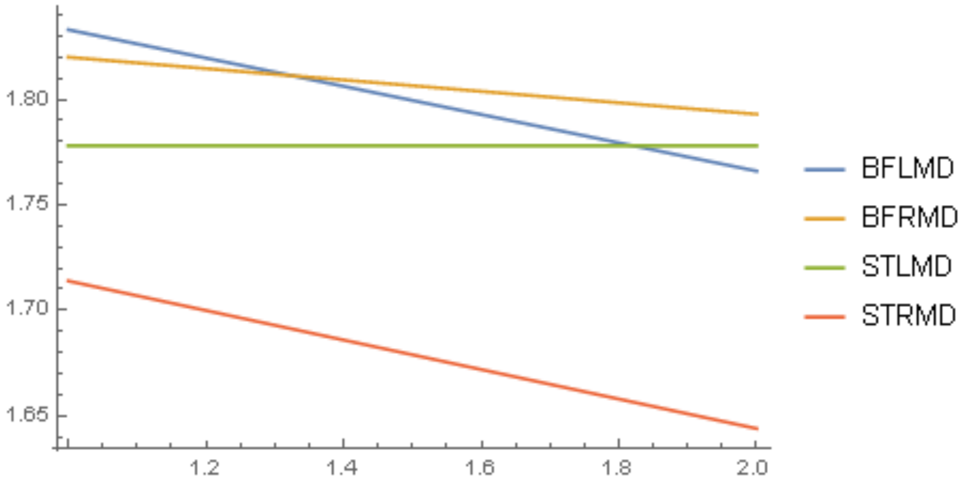
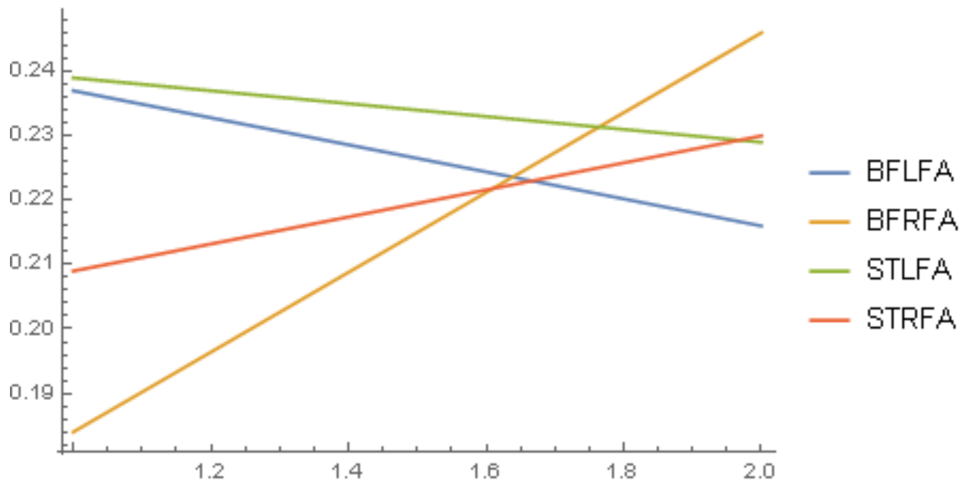


Fig 2. Fractional Anisotropy (FA) of 5 processed DTI MRI data sets with segmentation of the complete muscle



Conclusion

Current MRI DTI processing time per time point and per single is 30 hours. Current analysis showed that fibre tracking techniques for evaluating muscle fibres at return to play (RTP) are insufficient for accurately evaluation. New post-processing and segmentation methods are warranted for optimisation of DTI MRI muscle injury techniques.

Optimisation of the time-consuming data processing process is required for repeated analysis of the scans of includes athletes. Based on our result, **at this stage DTI MRI is a non-feasible technique for studying micro-structural recovery at return to play.**

These technical challenges will not affect our continuing recruitment process. Optimising of data processing is planned for the upcoming months with expected preliminary results in the Summer 2017.

T2 coronal images of included athletes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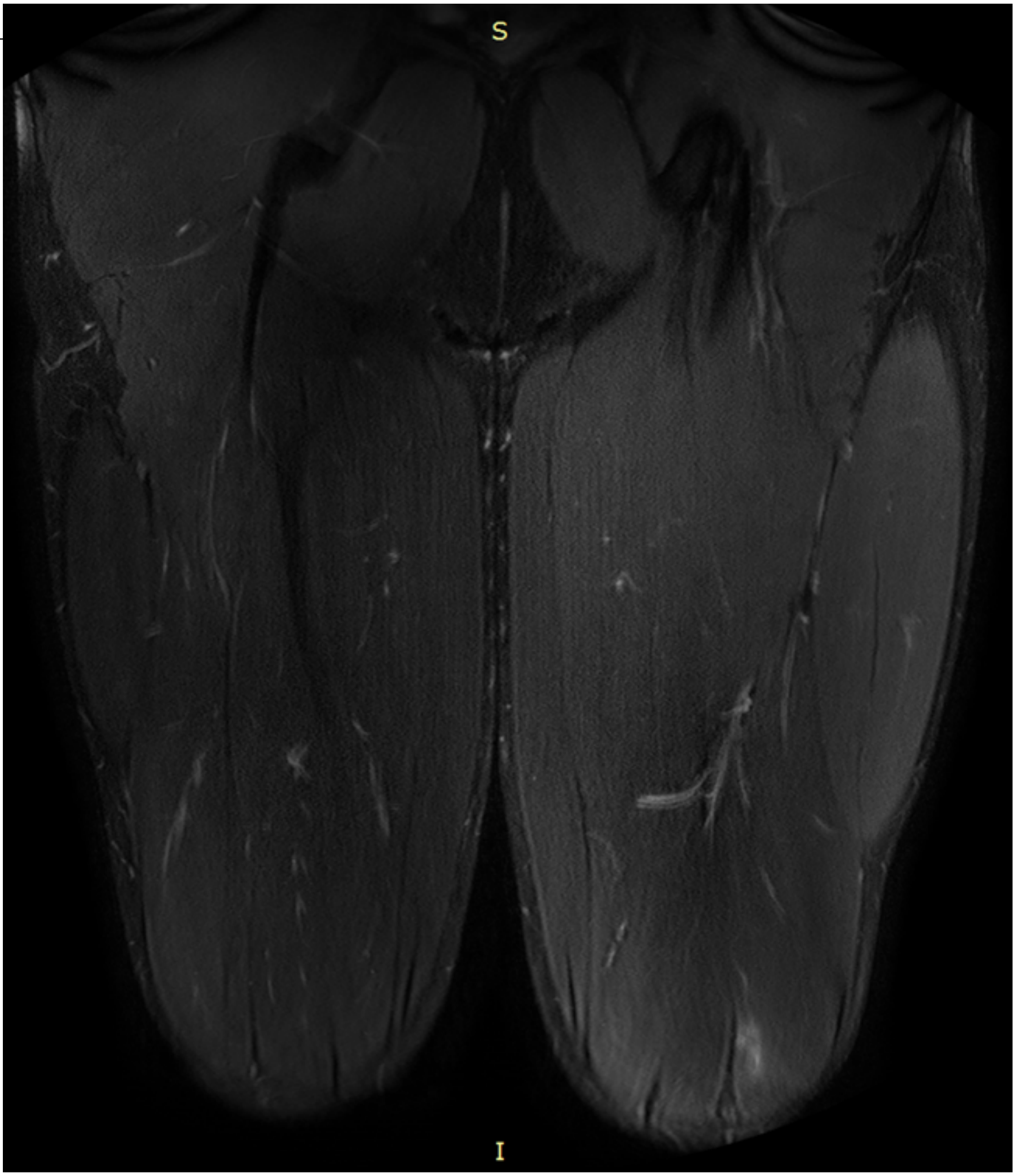
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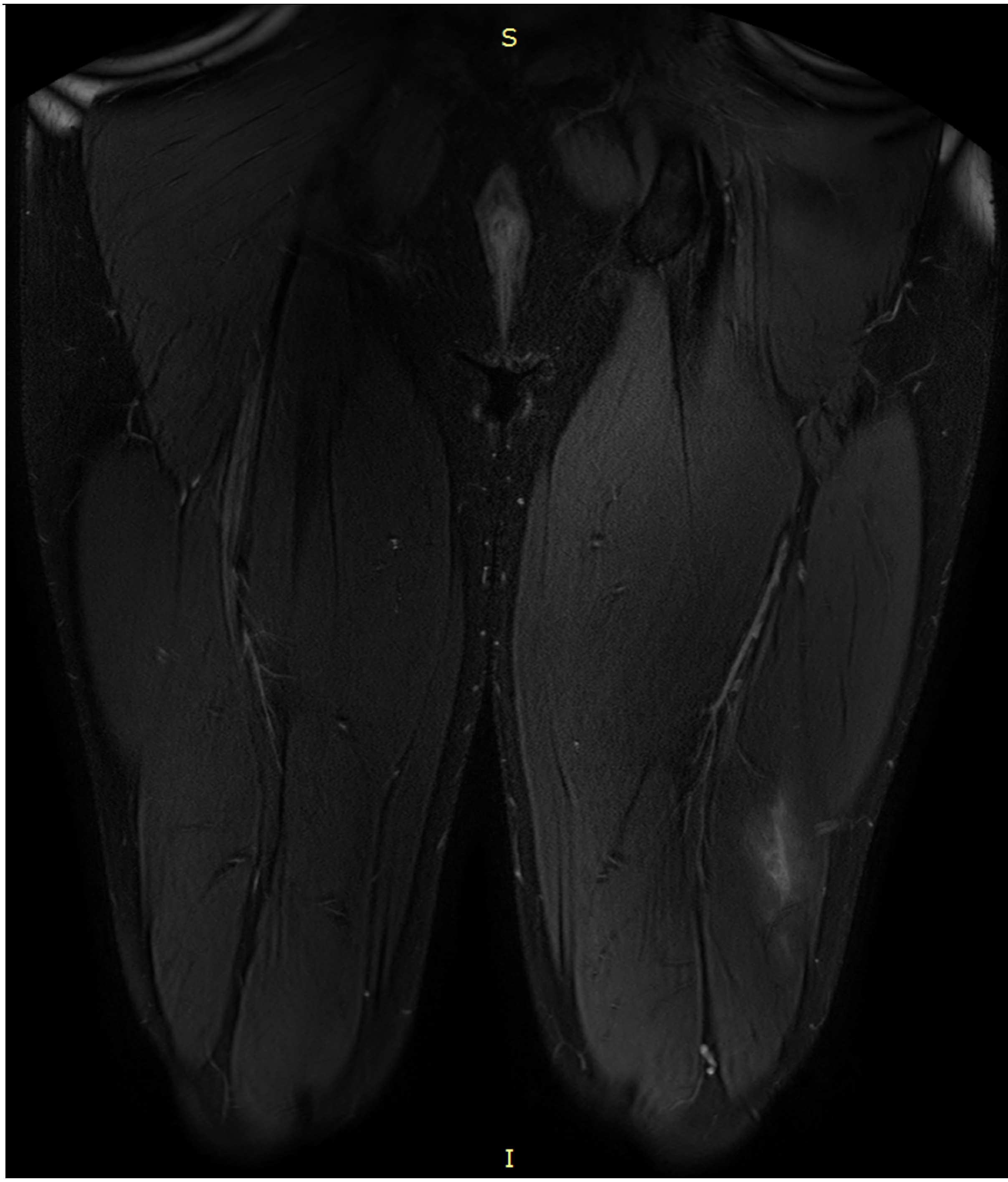
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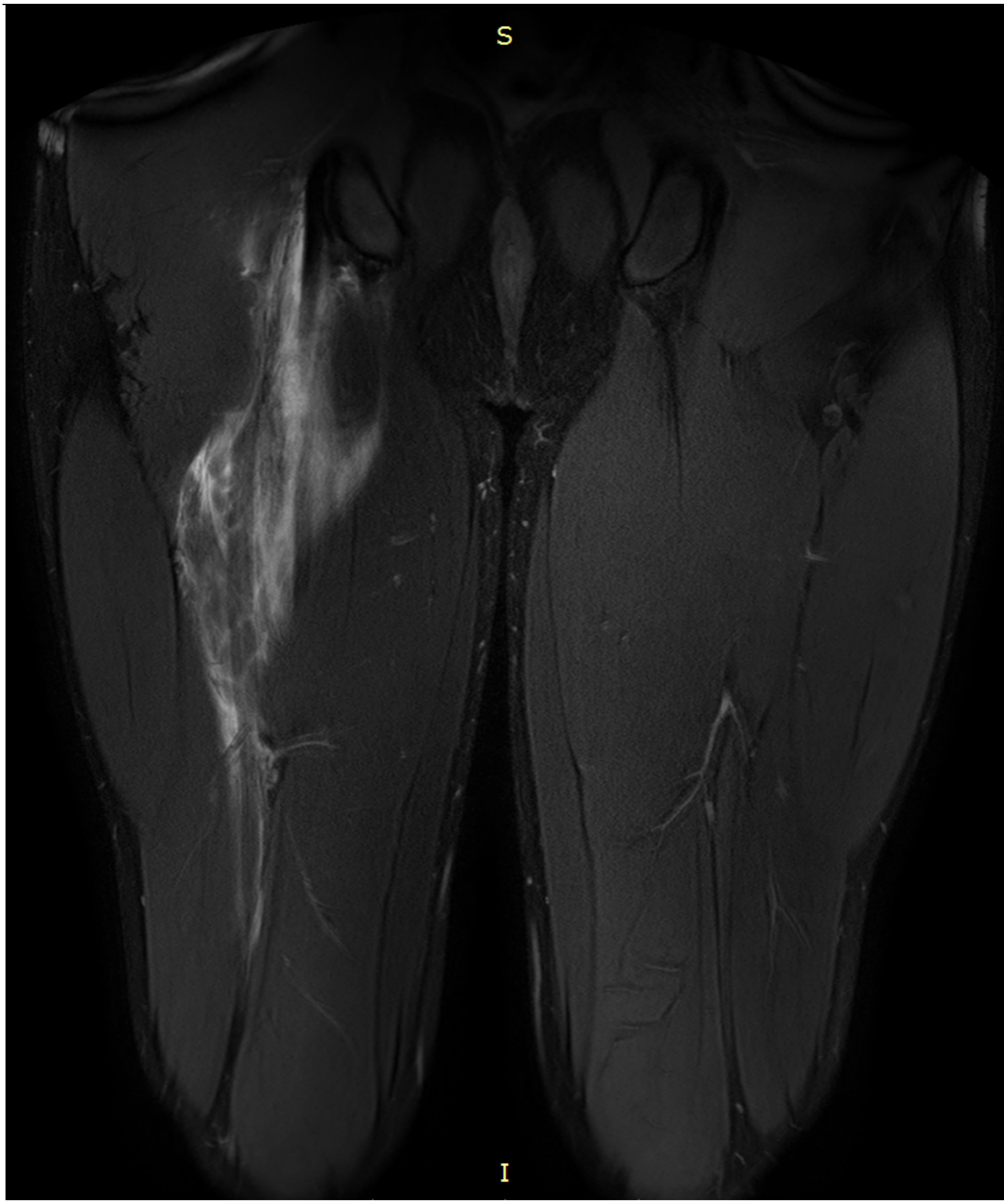
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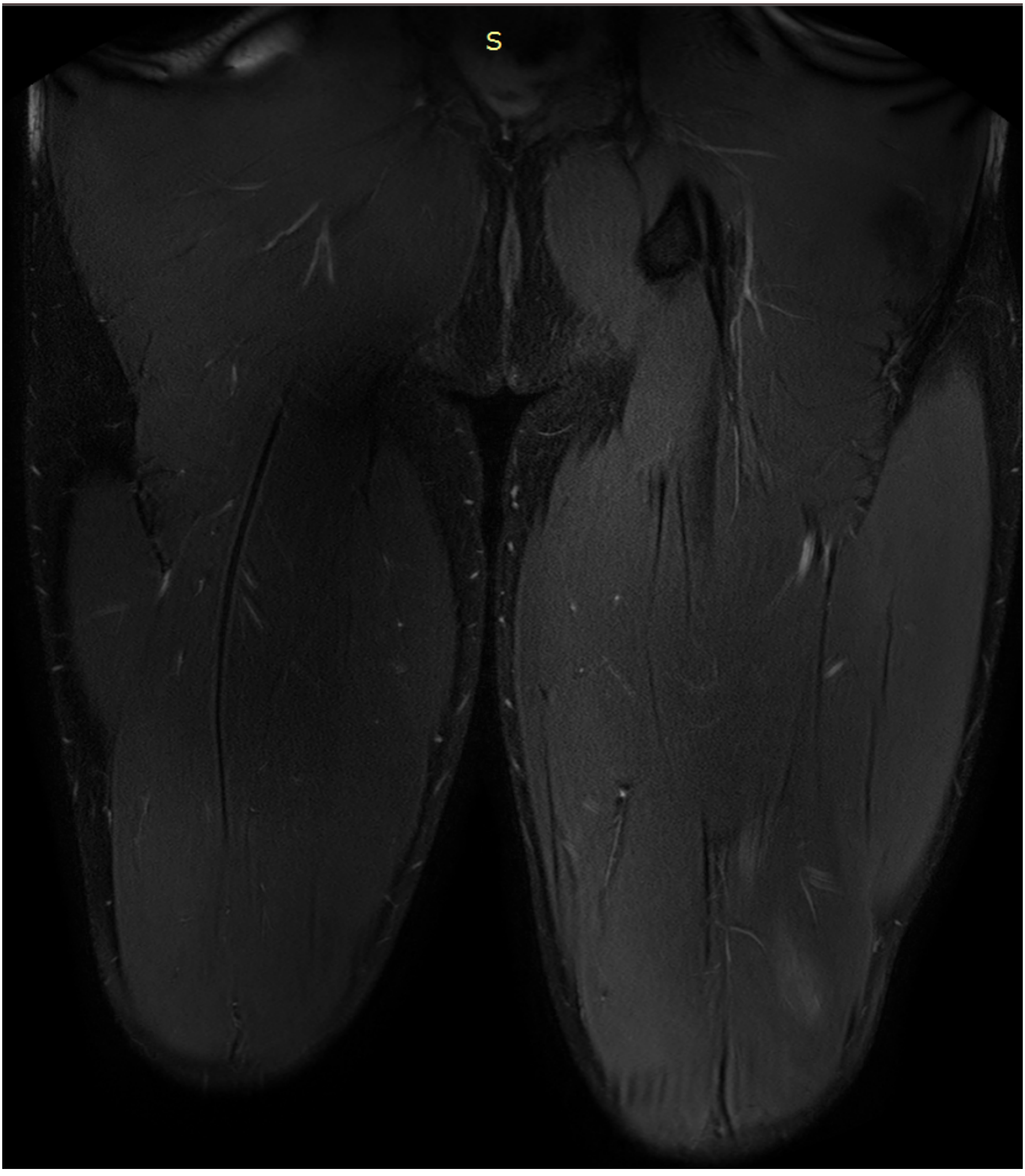
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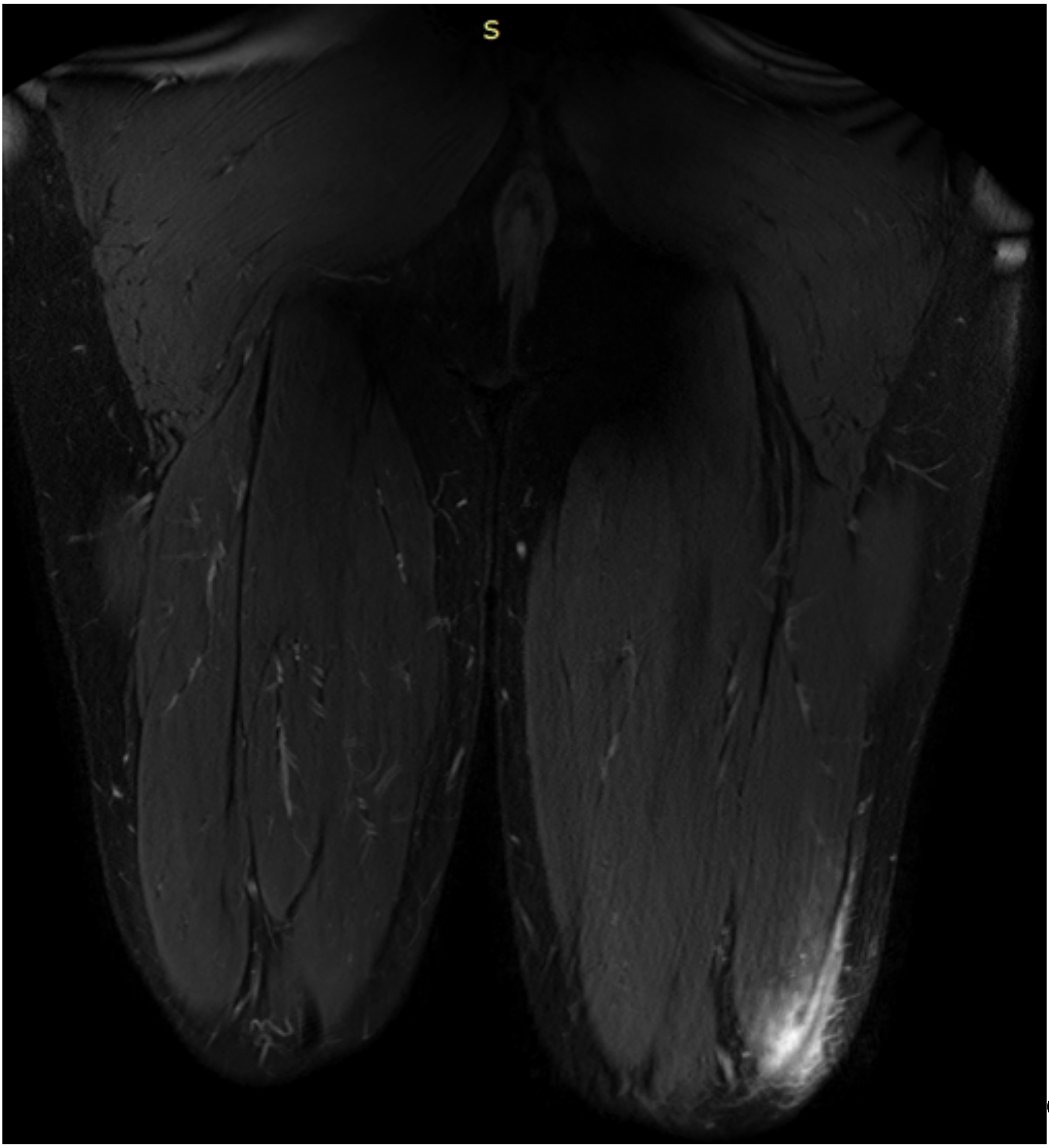
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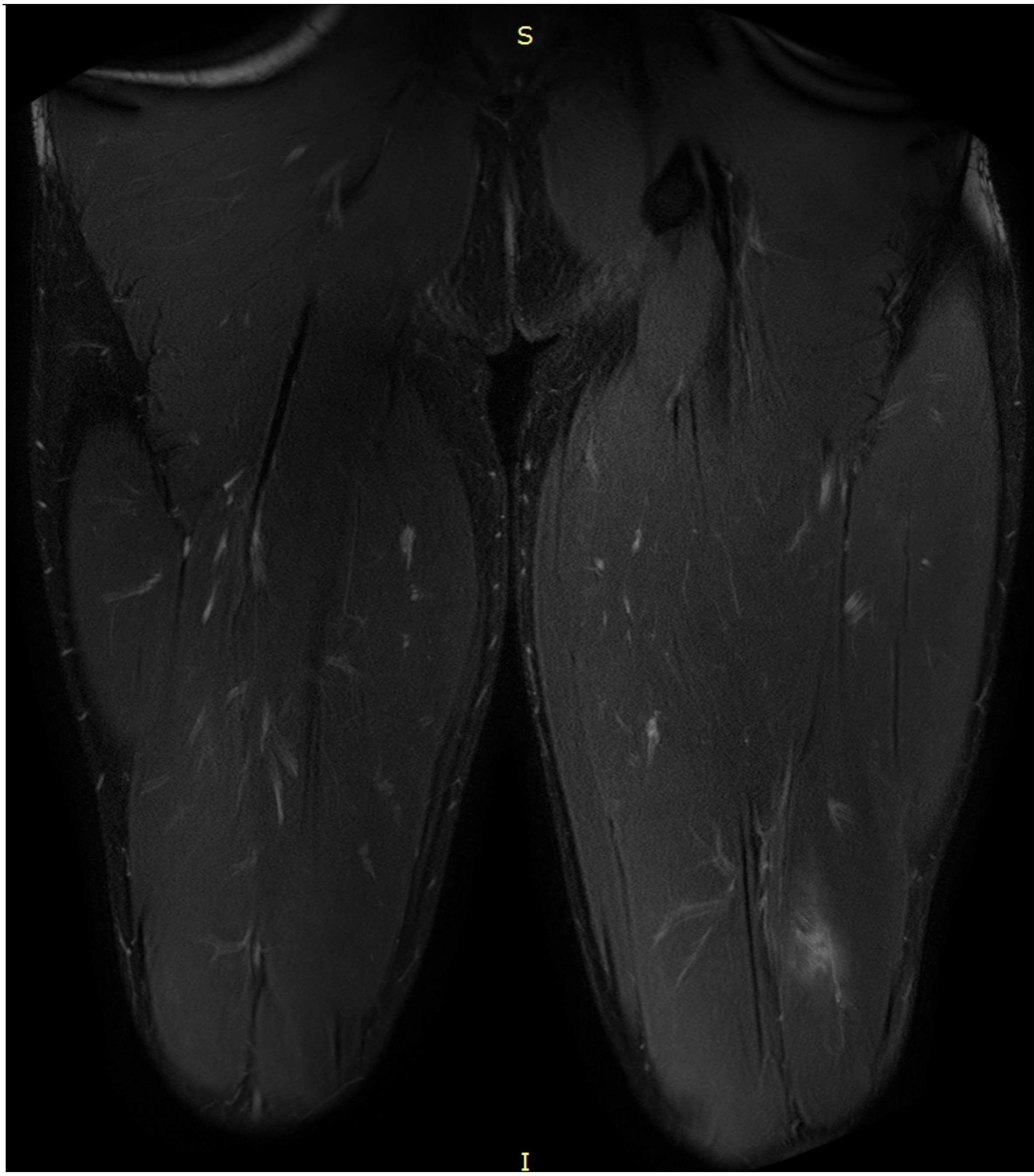
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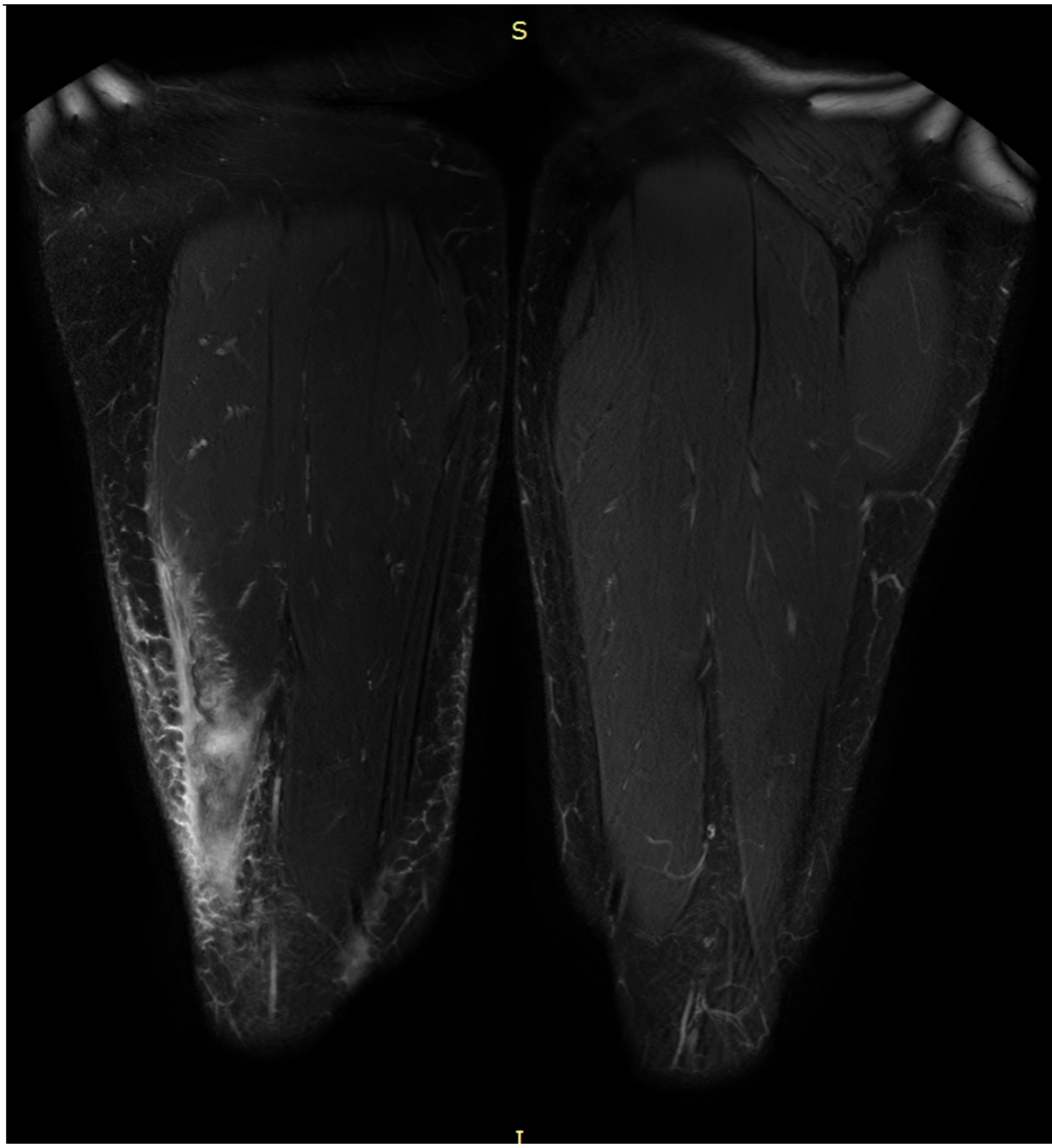
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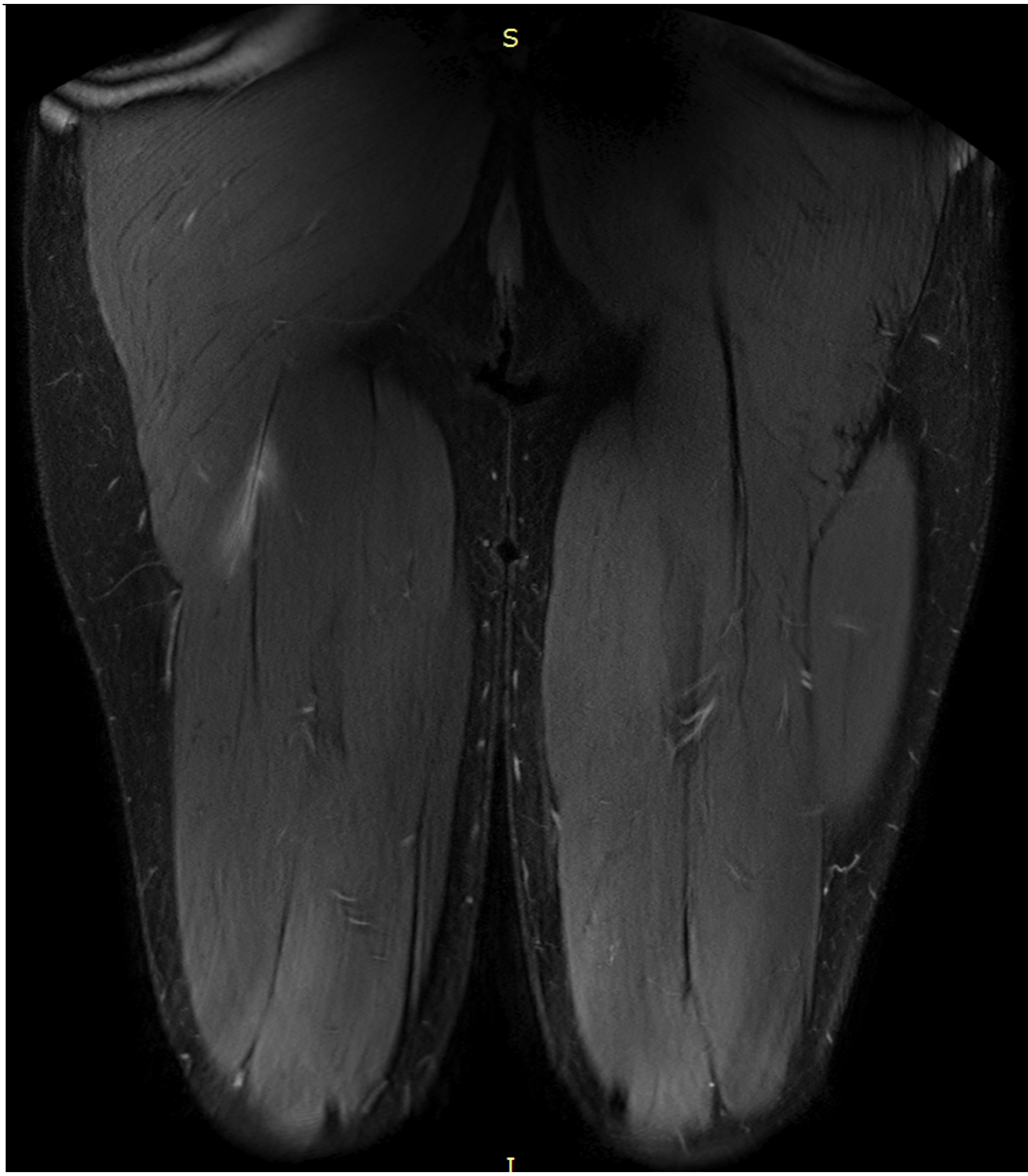
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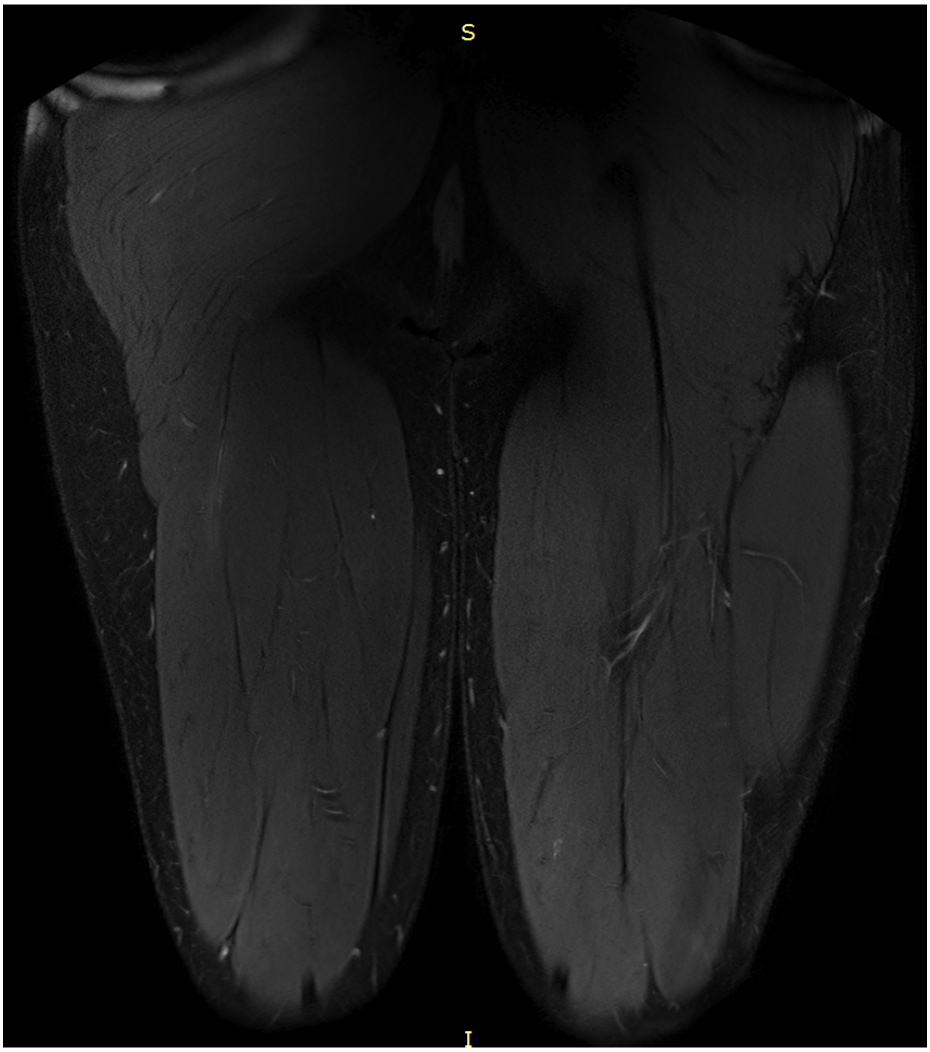
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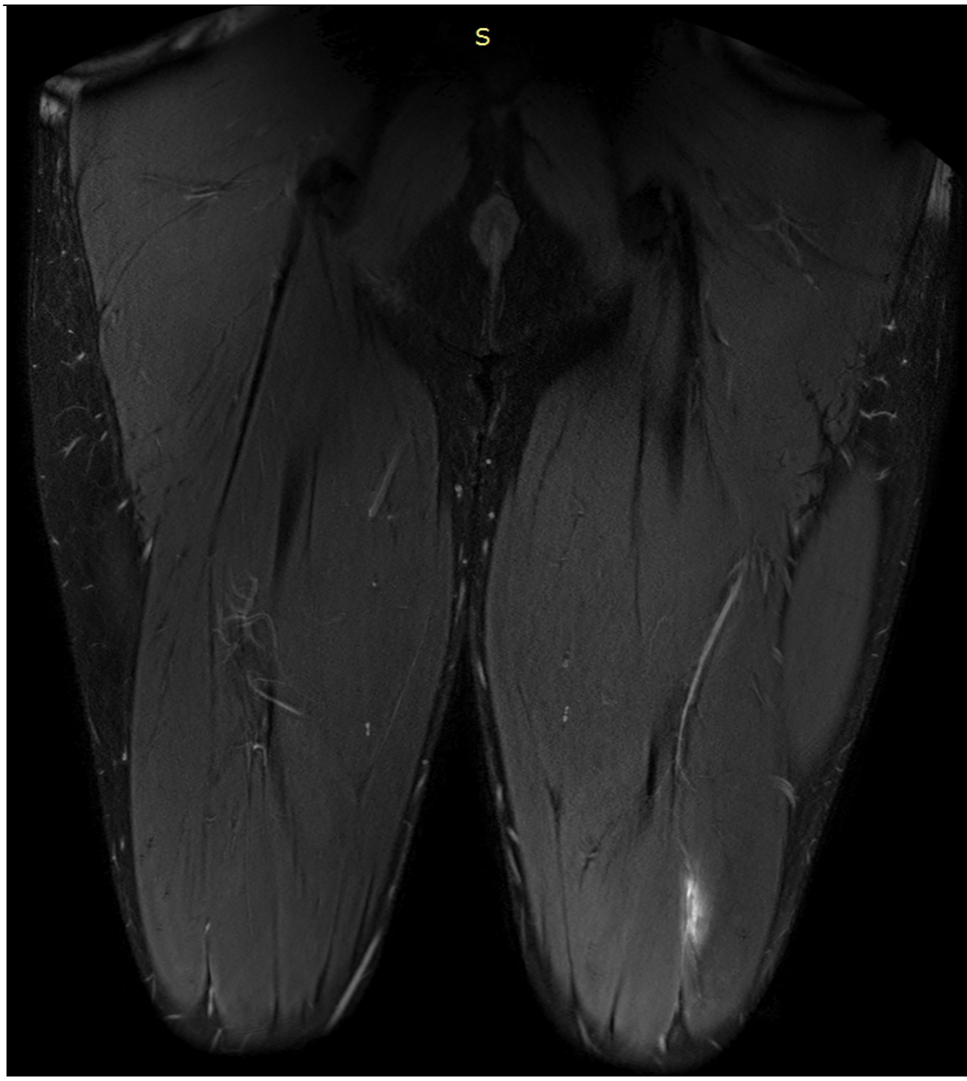
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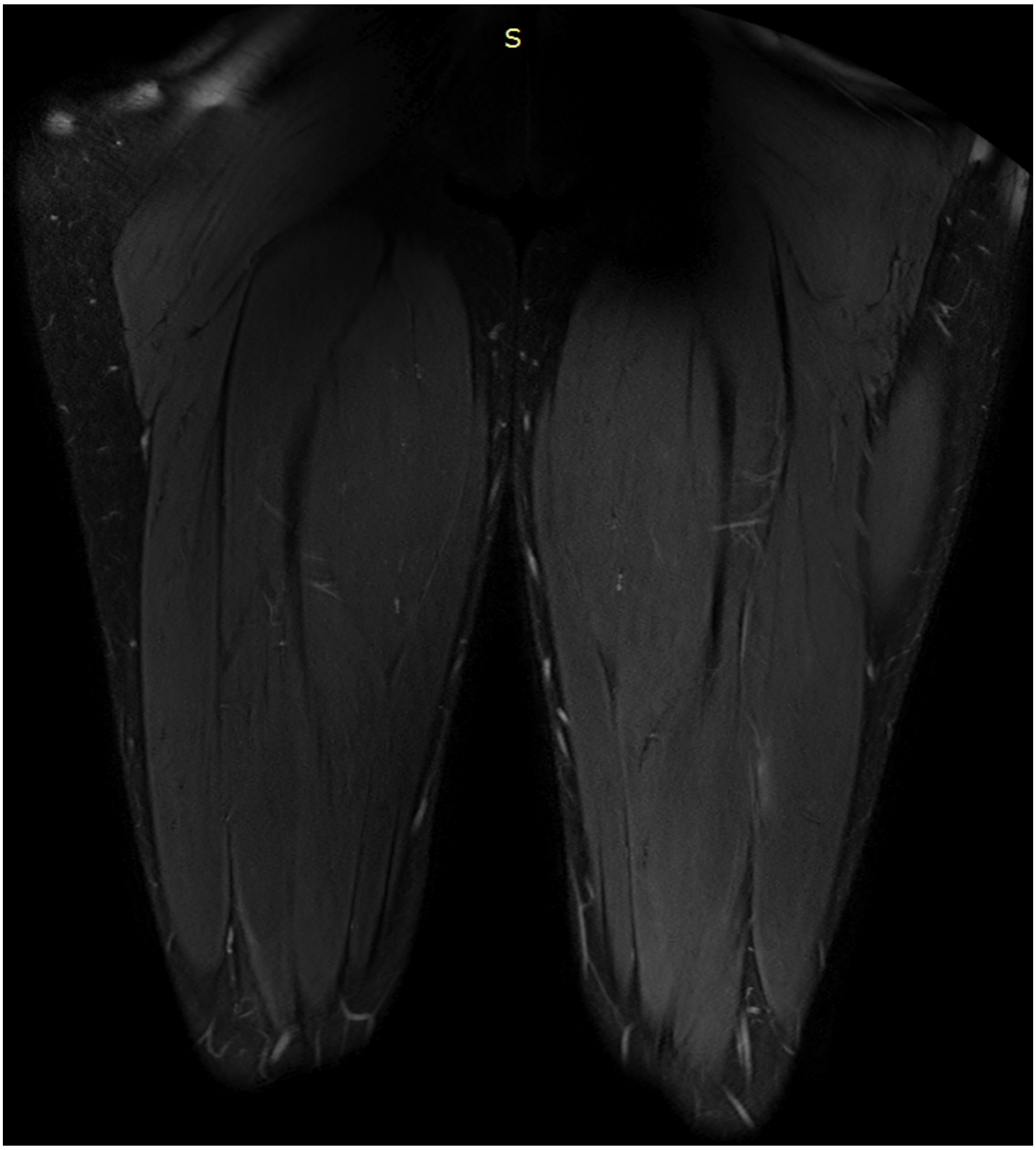
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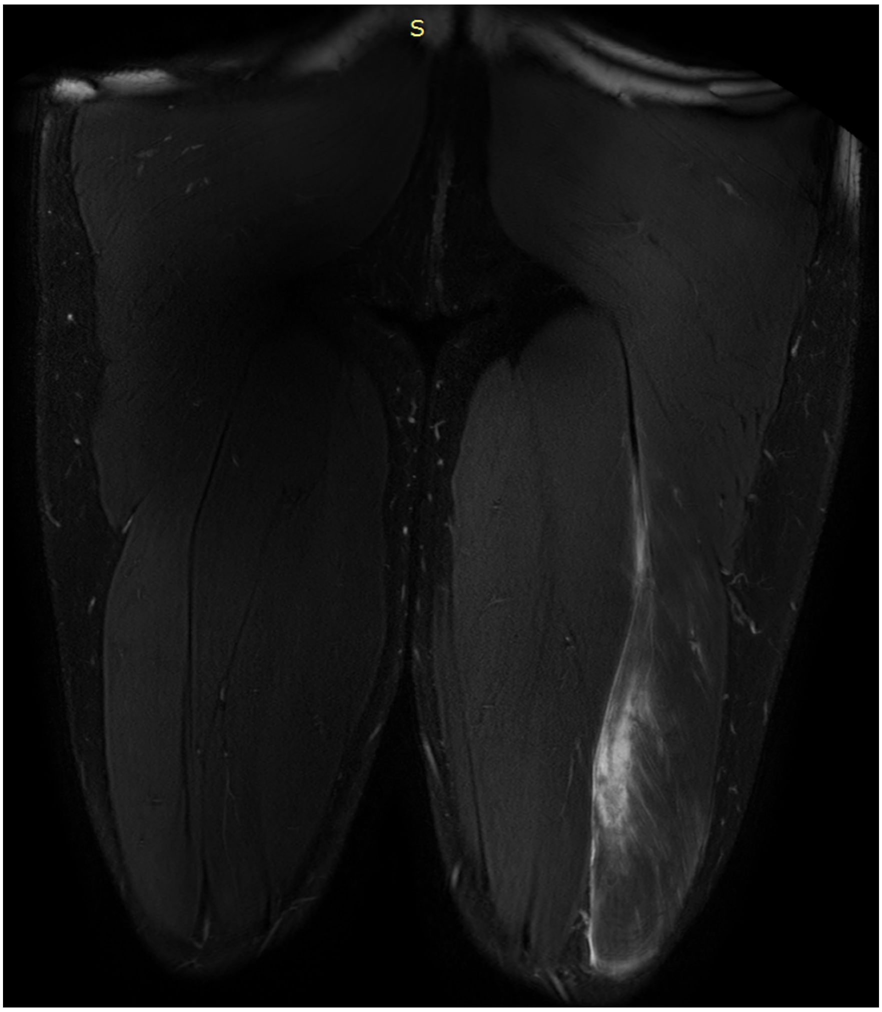
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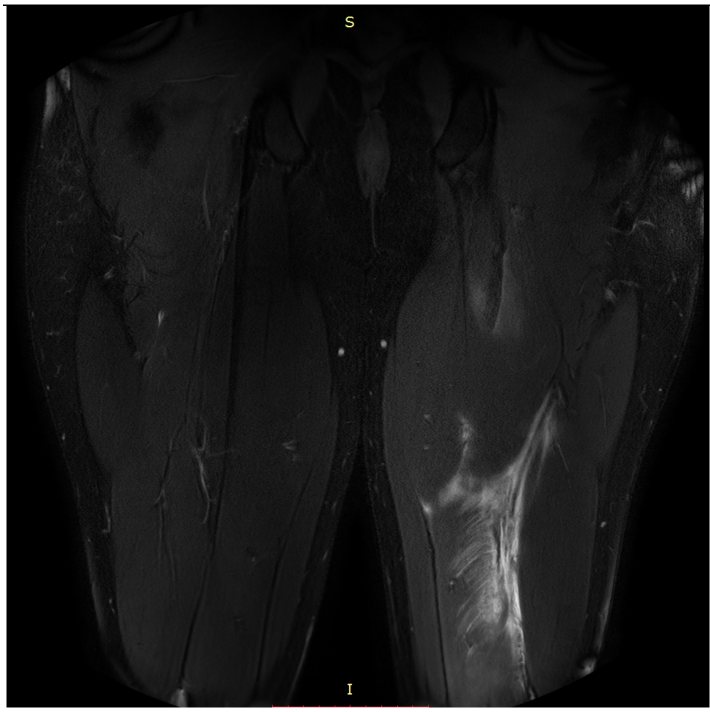
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