The Knee xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

The Knee

ACL graft metabolic activity assessed by ^{18}FDG PET–MRI

Robert A. Magnussen [a,b,*], Katherine Binzel [c,d], Jun Zhang [c,d], Wenbo Wei [c,d], Melanie U. Knopp [c], David C. Flanigan [a,b], Timothy E. Hewett [e], Christopher C. Kaeding [a,b], Michael V. Knopp [c,d]

[a] Department of Orthopaedics, The Ohio State University, Columbus, OH, United States
[b] OSU Sports Medicine, Sports Health and Performance Institute, The Ohio State University, Columbus, OH, United States
[c] Wright Center of Innovation in Biomedical Imaging, The Ohio State University, Columbus, OH, United States
[d] Department of Radiology, The Ohio State University, Columbus, OH, United States
[e] Department of Orthopedic Surgery, Mayo Clinic, Rochester, MN, United States

ARTICLE INFO

Article history:
Received 21 December 2016
Received in revised form 20 March 2017
Accepted 12 April 2017
Available online xxxx

Keywords:
ACL reconstruction
Ligamentization
Magnetic resonance imaging
Positron emission tomography
^{18}FDG

ABSTRACT

Background: To demonstrate the use of ^{18}Fluorodeoxyglucose positron emission tomography (PET) and magnetic resonance imaging (MRI) in combination (^{18}FDG-PET) to assess the metabolic activity of ACL graft tissue and evaluate the utility of this technique for ligament imaging.
Methods: Twenty-one knees with intact ACL grafts in 19 patients at multiple time points following ACL reconstruction were recruited to participate. PET–MRI imaging was performed using a custom device to place knees in the same position for both studies. Images were co-registered for quantification of ^{18}FDG-PET standardized uptake value (SUV) for the proximal, middle, and distal ACL was quantified. Signal in extra-articular muscle tissue in the index knee was also recorded as a control. Signal from each location was compared based on how far post-operative each knee was from ACL reconstruction (<6 months, six to 12 months, 12–24 months, or >24 months).
Results: Significant differences in ^{18}FDG PET SUV between the four time points were observed in the proximal ($p = 0.02$), middle ($p = 0.004$), and distal ($p = 0.007$) portions of the ACL graft. The greater than 24 months group was noted to be different from other groups in each case. No difference in PET ^{18}FDG SUV was noted in the extra-articular muscle in the index knee in each time group ($p = 0.61$).
Conclusions: Metabolic activity was noted to be significantly lower in grafts imaged greater than two years post-reconstruction relative to those grafts that had been in place for shorter periods of time.

1. Introduction

The anterior cruciate ligament (ACL) is commonly injured and is the most frequently reconstructed ligament of the knee. Modern techniques allow clinically stable ligament reconstruction in the majority of cases; however, failed reconstruction continues to be a problem with failure rates for ACL reconstruction reported to be between five and 20% [1,2].

While numerous factors likely contribute to this relatively high failure risk, the process of graft revascularization and ligamentization is crucial for a successful reconstruction. In order for a graft to function in the long-term, it must undergo

* Corresponding author at: 2835 Fred Taylor Dr, Columbus, OH 43202, United States.
E-mail address: robert.magnussen@osumc.edu (R. A. Magnussen).

http://dx.doi.org/10.1016/j.knee.2017.04.008
0968-0160/

ligamentization and become populated with living, metabolically active cells [3]. Numerous animal studies [4–6] and a magnetic resonance imaging (MRI) study [7] in humans demonstrate that the ligamentization process is quite variable among individuals and that complete ligamentization of the central portion may never occur in some cases [8]. Graft loading prior to adequate ligamentization may place the graft at increased risk for failure [3]. Given the different rates of ligamentization noted among individuals and the desire to return athletes to sport as early as possible, a tool that could quantify the revascularization and incorporation of an ACL graft would be highly useful.

Positron emission tomography (PET) scans have the capacity to quantify the metabolic activity of tissues [9]. This activity is assessed by the uptake of deoxyglucose labeled with a positron emitter (^{18}Fluorodeoxyglucose) (FDG). This glucose analogue cannot proceed through the Krebs cycle and remains in metabolically active cells for imaging. Recent innovations in image acquisition have improved PET detection sensitivity and precision of spatially resolved imaging while facilitating substantially lower radiotracer dose imaging [10]. Overlay of ^{18}Fluorodeoxyglucose (FDG) PET images onto MRI enables quantification of the metabolic activity of specific tissues (such as ligaments) with high resolution (Figure 1) [11,12]. No previous studies have evaluated the efficacy of ^{18}FDG PET–MRI scans to evaluate graft tissue following ACL reconstruction. The goals of this study were to demonstrate the use of PET–MRI to assess the metabolic activity of ACL graft tissue and evaluate the utility of this technique for ligament imaging. We hypothesized that ^{18}FDG-PET signal intensity of the ACL graft would be lower in patients for whom more time had passed since their ACL reconstruction.

2. Methods

Following approval from our institutional review board, 19 patients who had undergone previous ACL reconstruction (including two who had undergone bilateral reconstruction) were recruited to participate in this cross-sectional study. Chart review was undertaken to determine the time from ACL reconstruction to imaging for each knee and gather information regarding patient demographics and details of surgery. All reconstructions were performed with soft tissue grafts using suspensory fixation on the femoral side and interference screw and sheath fixation on the tibial side. Anatomic femoral tunnel placement was targeted in all cases using an outside-in or medial portal drilling technique. All patients were noted to have intact grafts on physical examination prior to study enrollment.

The 19 patients in the study included two patients with bilateral ACL reconstruction, yielding a total of 21 ACL-reconstructed knees for evaluation. The 19 patients had a mean age of 30.2 $\pm$ 9.7 years (range: 18.5–48.2 years) and included 17 males and two females. All knees were reconstructed with soft tissue grafts, including 16 hamstring autografts and five tibialis anterior allografts. Associated procedures at the time of ACL reconstruction included 12 partial meniscectomies (nine medial, three lateral) and four meniscus repairs (three medial, one lateral). The median time from ACL reconstruction to imaging in the 21 knees was 12.6 months (IQR (interquartile range): 8.2–19.7 months) with a range from 1.6 to 125.9 months. Time from reconstruction to imaging was less than six months in four knees, six to 12 months in seven knees, 12 to 24 months in five knees, and over 24 months in five knees.

MRI was performed on a 3 T system (Achieva, Philips Healthcare, Cleveland, OH) using an eight-channel phased array knee coil. MRI including proton density and T1 weighted sequences were acquired in three planes, with a three-dimensional (3D) high resolution image acquired in the sagittal plane. For the 3D volumetric acquisition, a single-shot T1 weighted fast field echo (FFE) sequence with fat suppression was implemented with FOV (field of view) = 170 $\times$ 170 mm^2, resolution = 0.5 $\times$ 0.5 $\times$ 3 mm^3, TR (repetition time)/TE (echo time) = 9.6/4.8 ms, NSA (number of signal averages) = 2, and SENSE (sensitivity encoding) factor = 2. PET imaging was performed following a low-dose computed tomography scan taken from the midthighs to the midcalves covering both knees. A specially made positioning device was used to place the knees into the same position to that used for MRI (Figure 2). Patients were injected with an average of 3.0 mCi [111 MBq] ^{18}F-Fluorodeoxyglucose which is an ultra-low tracer dose protocol. Dynamic ^{18}FDG PET data were acquired continuously in one minute frames for 75 min, with injection of the ^{18}FDG radiotracer occurring 15–30 s into the first dynamic acquisition. PET and MRI images were co-registered for quantification of the PET standardized uptake value (SUV) for specific structures within the knee using PET data from the 60–75 min post-injection reconstructed static

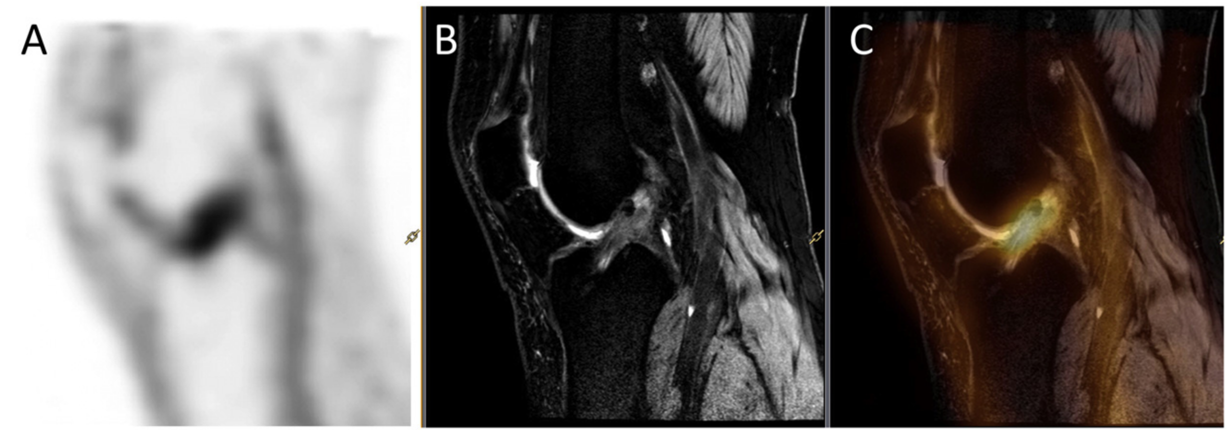

Figure 1. A) PET image, B) MRI image, and C) combined PET–MRI image of an ACL graft.