The use of diffusion weighted and dynamic contrast enhanced MRI for quantitative evaluation of the tibial tunnel after anterior cruciate ligament reconstruction with intraoperatively administered platelet-rich plasma gel

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Purpose

Methods have been sought to shorten the time for the anterior cruciate ligament (ACL) graft to acquire biomechanical properties similar to original ACL. The purpose of the study was to quantitatively evaluate the effect of platelet-rich plasma gel (PRPG), locally administered during the ACL reconstruction, with diffusion-weighted (DWI) and dynamic contrast-enhanced (DCEI) MRI.

During the physiological cascades of soft tissue healing and bone growth, cellular and hormonal factors play an important role, the most important among them being various growth factors [1]. Platelet-rich plasma (PRP), defined as a portion of the plasma fraction of autologous blood having a platelet concentration above the baseline, contains an autologous concentration of platelets and growth factors [2]. PRP can be activated with thrombin to create platelet-rich plasma gel (PRPG). MRI proved to be an excellent noninvasive tool for the qualitative evaluation of oedema and vascularity, which are both present during graft healing. Quantitative MRI sequences such as DWI and DCEI can provide additional quantitative information on these processes.
Methods and Materials

In fifty patients, the standard arthroscopic reconstructive procedure, using the single-incision technique with a double-looped semitendinosus and gracilis tendon graft was performed. The patients in the PRPG group (n =25) received a local application of PRPG into the bone tunnels and into the graft itself.

MRI scans were performed on a 1,5 T MRI scanner one, two and a half and six months after the ACL reconstruction.

DWI was performed with the echo-planar imaging method, using the spin-echo single shot technique at TR/TE = 8000/75 ms. Two image acquisitions were performed for each DWI method: one without (b=0 s/mm²) and the other with diffusion weighting (b=400 s/mm²). The area of proximal tibia was examined with transverse slices perpendicular to the tibial tunnel (Fig 1a,b).

DCEI was performed by the EFGRE3D method. The paramagnetic contrast medium (CM) was administered i.v. using an MR injection system in a concentration of 0.1 mmol/kg body weight at a 3 ml/s flow rate, followed by an injection of 20 ml saline at the start of the first DCEI series. Images were acquired dynamically through the proximal tibia perpendicular to the tibial tunnel every 16 seconds in 25 time frames (Fig 2a,b).

In postprocessing, a region of interest (ROI) encircling the tibial tunnel in a slice at a mid-distance between the plateau and the interference screw was examined.

ADC maps were calculated from the two DWI image sets of different b values. This was followed by calculation of ADC values for the selected ROI.

Each DCEI measurement yielded a signal intensity (SI)-time curve (Fig 2c) and the mathematical model was fitted to the measured data to a model function given by the equation: SI=SI₀+(SIₘₐₓ-SI₀)(1-exp(-t/#)). SI₀ represents the SI at the start of the first DCEI series, which then exponentially approaches maximum signal intensity SIₘₐₓ in the characteristic time for the SI increase #. Finally, two characteristic parameters were extracted form the previous formula: the enhancement gradient (Gₐₑｎ₉) and the enhancement factor (Fₑₑｎ₉). The enhancement gradient Gₑₑₙ₉=100((SIₘₐₓ-SI₀)/(SI₀#)) yields a relative SI increase per unit time and therefore represents the enhancement rate, while the enhancement factor Fₑₑₙ₉=(SIₘₐₓ-SI₀)/SI₀, which is a dimensionless quantity, describes the amount of contrast accumulated in ROI compared to the baseline [3].
Fig. 1: Quantitative MRI assessment of the tibial tunnel with DWI. Two oblique paraaxial diffusion weighted images perpendicular to the tibial tunnel at half the distance between the tibial plateau and the tip of the screw performed at different diffusion strengths: (a) $b=0$ s/mm² and (b) $b=400$ s/mm², are shown. Regression analysis of both images allowed the ADC value calculation for the selected region of interest (ROI).

**Fig. 2:** Quantitative MRI assessment of the tibial tunnel with DCEI. The first (a) and the last (b) perpendicular image of the tibial tunnel of the stack of 25 successive dynamic contrast-enhanced images after i.v. contrast medium (CM) administration. Note the hyperintense interface zone in the encircled ROI (b) compared with the first image of the stack (a) at the start of CM administration. (c) Signal intensity (SI)-time curve for the same patient (diamond) along with corresponding curve of the model function (solid black line), showing an increase in the SI values (y axis) at the time interval of 16 seconds (x axis) in the ROI.

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Results

The ADC values as well as $G_{\text{enh}}$ and $F_{\text{enh}}$ values decreased in each group during the follow-up.

At one month, the calculated average ADC value in the PRPG group was significantly lower than in the control group (Fig 3). At one and two and a half months, $G_{\text{enh}}$ was significantly higher in the PRPG group than in the control group (Fig 4). Average $F_{\text{enh}}$ was at all control examinations higher in the PRPG group than in the control group, although not statistically significantly (Fig 5).
Fig. 3: Apparent diffusion coefficient (ADC) values in both groups during the follow-up. Values are presented as mean (standard error). ADC values in the PRPG group are lower at all follow-up examinations, although only at one month significantly.

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**Fig. 4:** Enhancement gradient (Genh) values in both groups, are presented as mean (standard error). Note significantly higher values in the PRPG group at first and second control examination, representing steeper signal intensity increase and therefore indicating higher vascular density in the ROI.

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Fig. 5: Enhancement factor (Fenh) values in both groups are presented as mean (standard error). Values are higher in the PRPG group at all follow-up controls, although not statistically significantly.

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Conclusion

After the reconstruction, graft healing in the tibial tunnel starts as an acute inflammatory response with oedema, neutrophils and recruited macrophages. In the chronic phase of inflammation, monocytes and stem cells initiate angiogenesis and the formation of a hypervascular granulation tissue interface between the graft and the host bone [1].

For ethical reasons, histological evaluation of ACL graft incorporation in humans is impossible. There have been only a few histological studies describing oedema and vascularity [4]. However, angiogenesis is an important part of graft incorporation, particularly in the early phases [4].

The ADC values as well as $G_{\text{enh}}$ and $F_{\text{enh}}$ values decreased in each group during the follow-up, presumably due to the histologically proven cellular proliferation during fibrous granulation tissue production in the process of graft healing [5].

The significantly lower ADC values in the ROI for the PRPG group at one month indicate additional decreased water mobility in the extracellular space and therefore also the oedema, suggesting a higher cellularity in the tunnel in this group [6]. This is consistent with histologically proven higher collagen fibril amount as the effects of PDGF some weeks after reconstruction [7].

The significantly larger $G_{\text{enh}}$ in the PRPG group at the first and second postoperative controls can be attributed to a faster inflow of CM, which is influenced mainly by vascular density [3]. This finding is in agreement with histological evidence of significantly higher vascular density in animal grafts after local PDGF administration [7].

Obviously, although not significantly higher values of the $F_{\text{enh}}$, in the PRPG group at the first and second controls could possibly be attributed to a small number of patients. On the other hand, this lack of significance could also indicate that for the assessment of vascularity the slope of the SI-time curve is even more sensitive than its peak [3].

To conclude, in our study, quantitative DWI and DCEI measurements indicated a reduced extent of oedema during the first postoperative month as well as an increased vascular density and microvessel permeability in the proximal tibial tunnel at one and two and a half postoperative months as the effect of the local application of PRPG.
References


