Chitosan-platelet-rich plasma implants have *in situ* tissue building capacity and can be injected into meniscus defects to improve repair

A Chevrier[1], G Deprés-Tremblay[1], M Nelea[1], M Hurtig[2] and MD Buschmann[1,3]
[1]Chemical Engineering Department and [3]Biomedical Engineering Institute, Polytechnique Montreal, Montreal, QC, Canada
[2]Department of clinical studies, University of Guelph, Guelph, ON, Canada

Main topic: Basic science
Second topic: Cartilage and meniscus

Purpose: The purpose of this study was to investigate the tissue building capacity of chitosan-PRP implants and whether these implants can improve repair in a sheep meniscus defect model.

Materials & Methods: Several polymer formulations containing a chitosan, an excipient (as lyoprotectant), as well as calcium chloride (as clot activator) were freeze-dried. Freeze-dried formulations were reconstituted in autologous leukocyte-rich PRP for dorsal subcutaneous injections into New Zealand White rabbits (n=11) to assess the implants' *in situ* tissue building capacity. In addition, bilateral 10-mm defects were created in the anterior portion of the medial meniscus in skeletally mature sheep (n=11). Chitosan-autologous PRP implants were injected into the defects through 2 trephination channels and the tears were sutured. Implant retention was assessed at 24 hours and repair was assessed at 3 weeks and 3 months. Controls were recalcified PRP.

Results: Freeze-dried chitosan formulations were solubilised in autologous PRP and injected subcutaneously into NZW rabbits where they solidified to form stable implants (Fig. 1 a to c). Chitosan-PRP implants were resident until at least 14 days (Fig. 1 a to c), while PRP controls were quickly degraded (Fig. 1d). Chitosan-PRP implants induced cell recruitment (Fig. 1 a, b, c, e&f) and angiogenesis (Fig. 1 g&h) *in situ*. Chitosan-PRP implants were injected into meniscus defects through trephination channels and were resident for at least 24 hours, even without immobilizing the sheep's legs in a cast (Fig. 2 a to d). Biochemical and histological analyses of meniscal repair tissues and articular surfaces at 3 weeks and 3 months are ongoing (Fig. 2e).

Conclusion: Freeze-dried chitosan formulations can be solubilised in autologous PRP to form injectable implants that have *in situ* tissue building capacity. Chitosan-PRP implants can be injected into meniscus defects and are expected to improve repair outcomes and restore meniscus function.

Keywords: Chitosan, platelet-rich plasma, injectable implants, meniscus repair

Figures:

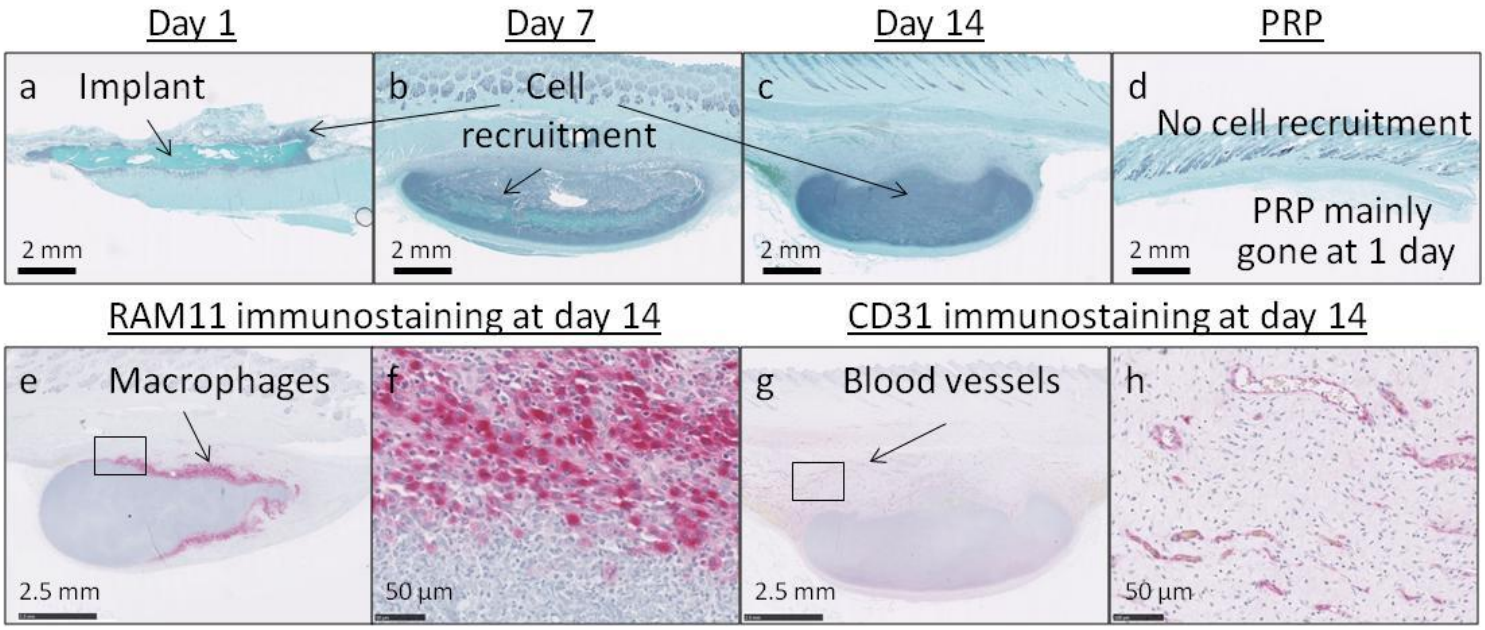

Figure 1. Chitosan-PRP implants were injected subcutaneously into NZW rabbits and were resident *in vivo* for at least 14 days (a to c), while PRP controls were quickly degraded (d). Chitosan-PRP implants had *in situ* tissue building capacity, induced cell recruitment (a, b, c, e&f) and angiogenesis (g&h). Rectangles in panels e&g indicate regions where the higher magnification images f&h were taken.

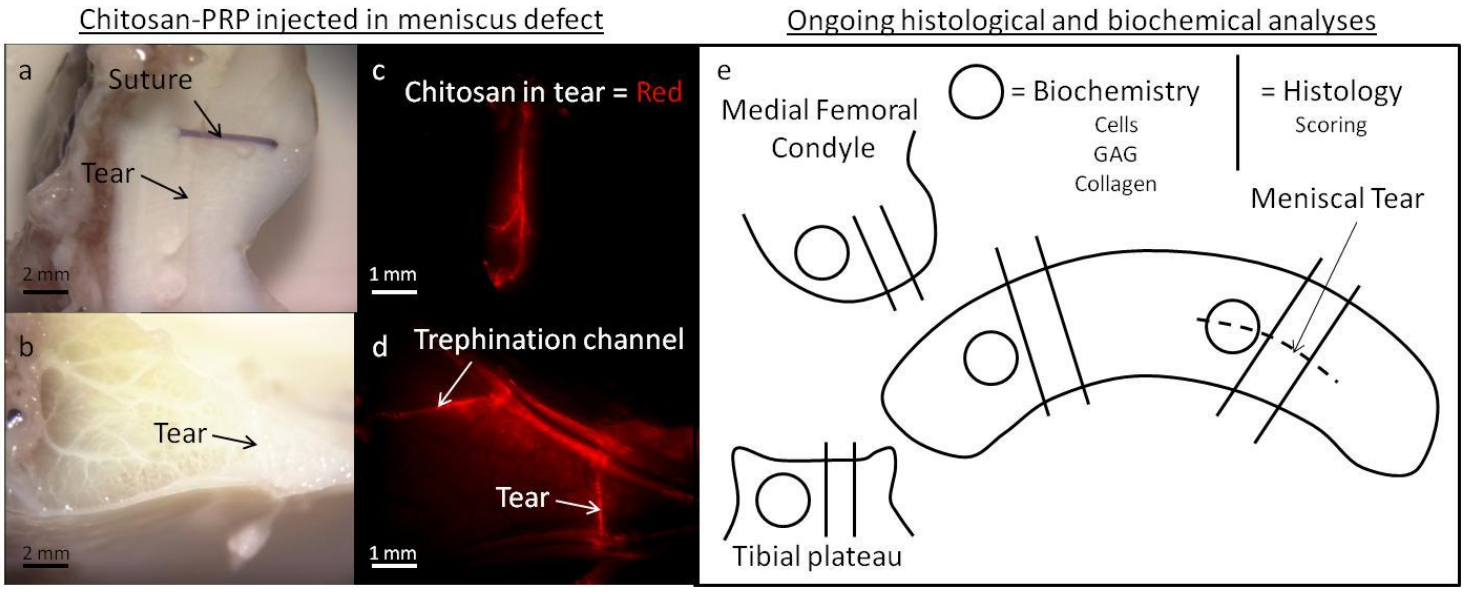

Figure 2. Chitosan-PRP implants were injected into sheep meniscus defects through trephination channels and were resident for at least 24 hours, even without any post-operative immobilization (a to d). Schematic representation of ongoing histological and biochemical analyses (e). Chitosan can be detected with red fluorescent microscopy in panels c&d since a rhodamine-chitosan tracer of similar M_n was added to the chitosan-PRP formulation for imaging purposes.