

## Freeze-dried chitosan-PRP implants improve meniscus repair in an ovine model

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*Main topic: Basic science*

*Second topic: Cartilage and meniscus*

**Purpose:** The purpose of this study was to investigate whether surgical repair of ovine meniscus tears can be augmented by applying chitosan-PRP implants and wrapping the meniscus with a collagen membrane.

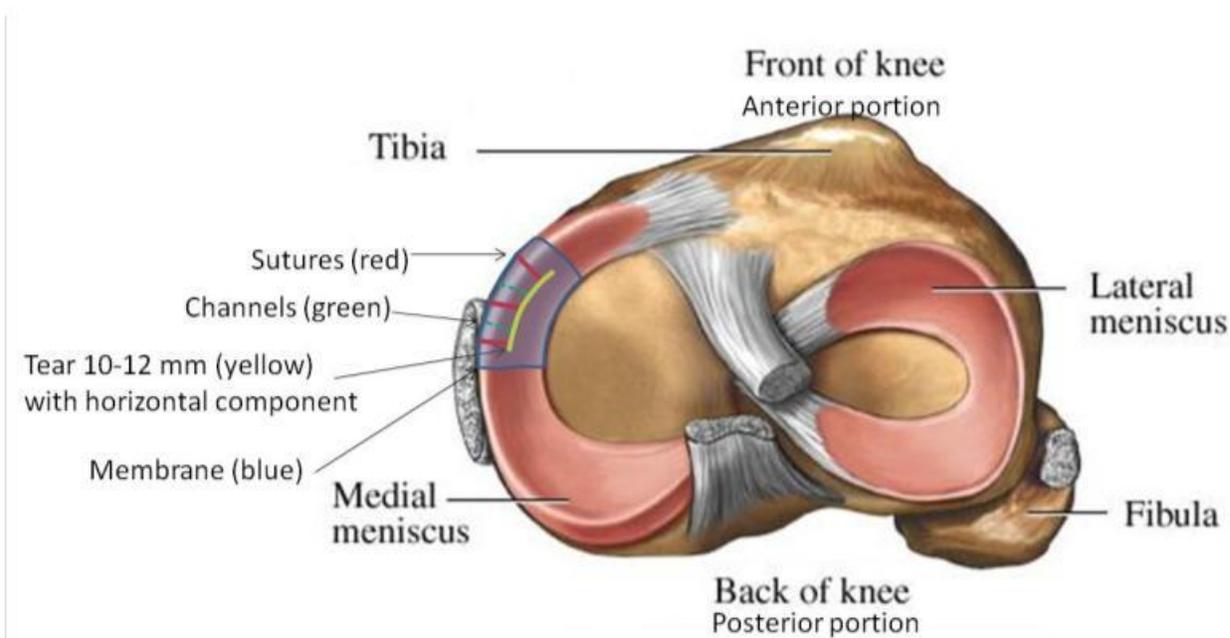
**Materials & Methods:** Formulations containing 1% (w/v) chitosan (80% DDA and  $M_n$  40 kDa), 1% (w/v) trehalose (as lyoprotectant) and 42.2 mM calcium chloride (as clot activator) were freeze dried and solubilized in autologous PRP immediately prior to application. Unilateral 10 mm longitudinal tears were created in the medial meniscus of six skeletally mature ewes and treated by suturing and either injecting chitosan-PRP in the tear (n=2), wrapping the meniscus with a collagen membrane and injecting chitosan-PRP in the tear and under the wrap (n=2) or wrapping only (n=2) (**Fig 1**). Tissue repair was histologically assessed at 6 weeks.

**Results:** Complete healing and seamless integration were observed in one chitosan-PRP treated tear (**Fig 2 a&b**), while there was partial healing in one tear treated with chitosan-PRP and wrapping (**Fig 2 c&d**). The repair tissue was highly cellular and well integrated to surrounding host meniscus (**Fig 2 a to d**). Intact menisci were structurally different in matching areas (**Fig 2 g&h**). There was no healing in the menisci treated with wrapping alone (**Fig 2 e&f**). Significant cell infiltration was observed at the outer portion of all torn and treated menisci (**Fig 2, compare a, c, e, vs g**). Suture tracks were abundant in menisci treated with the wrapping technique (**Fig 2 c&e**).

**Conclusion:** Chitosan-PRP implants showed superior regenerative effect compared to wrapping the meniscus with a collagen membrane. Using the wrap in conjunction with chitosan-PRP implants did not further improve repair and the additional sutures needed to secure the wrap created significant damage to the menisci. This suggests that chitosan-PRP implants by themselves could be efficient in overcoming the current limitations of meniscus repair.

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

## a) Schematic representation of the model

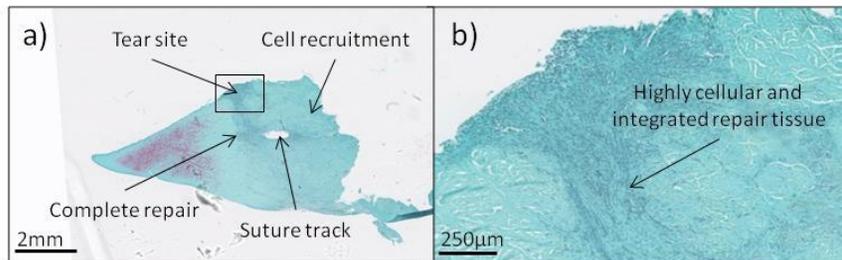


## b) Study design

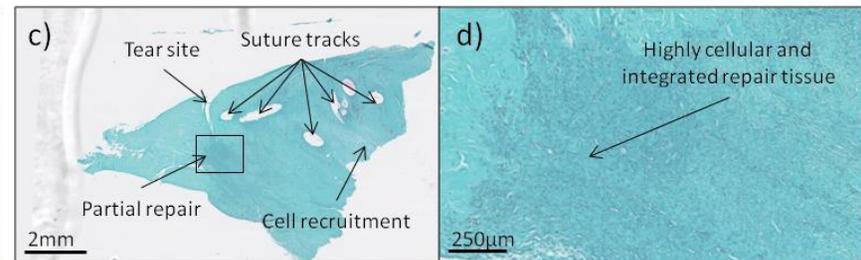
Group	Test Article	Total Volume Implant (mL)	# Animals / time points
1	CS-PRP with wrapping	0.5 mL in the tear + 0.5 mL under membrane	n = 2 at 6 weeks
2	Wrapping only	None	n = 2 at 6 weeks
3	CS-PRP only	0.5 mL in the tear	n = 2 at 6 weeks

**Figure 1. a)** Schematic representation of the surgical model. A bone block with medial collateral ligament attached was extracted to increase access to the meniscus. A 10 mm longitudinal tear with a horizontal component was created towards the anterior portion of the medial meniscus (**in yellow**). Two 20-gauge needles were used to create trephination channels from the capsular border of the meniscus to the tear (**in green**). 0.5 mL chitosan-PRP implant was extruded into the tear via the trephination channels and the tear was stabilized with three sutures tightened in a vertical pattern (**in red**). A piece of collagen membrane (12.5 mm X 25 mm) was wrapped around the meniscus (**in blue**) and sutured first at the capsular border, and then with two vertical sutures placed through the meniscal tissue. 0.5 mL chitosan-PRP implant was injected under the membrane. The contralateral knee was left intact. **b)** Study design. Six ewes (2-6 years old) were included in the study and treated with either chitosan-PRP with wrapping (n = 2), wrapping only (n = 2) or chitosan-PRP only (n = 2).

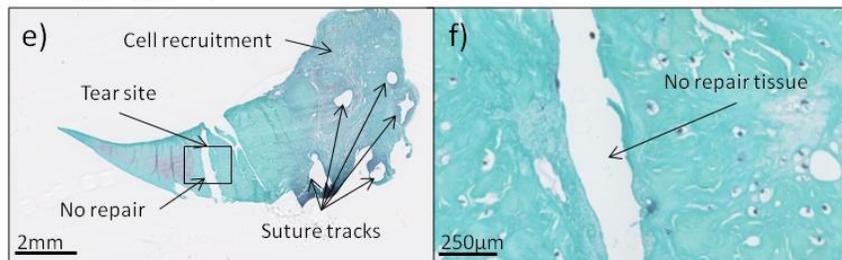
### CS-PRP only



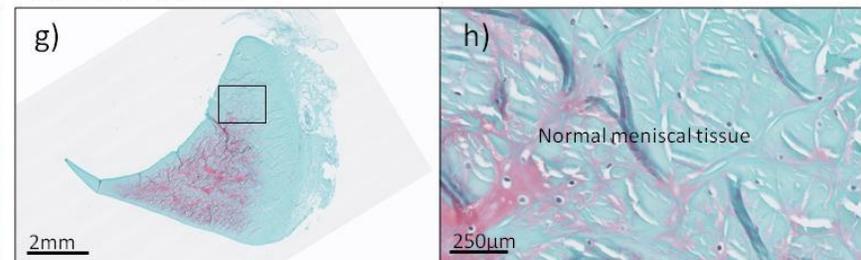
### CS-PRP with wrapping



### Wrapping only



### Intact meniscus



**Figure 2.** Safranin O/Fast Green-stained coronal sections of menisci were used to evaluate tissue repair after 6 weeks. One tear treated with chitosan-PRP only showed complete repair (a, b), while one tear treated with chitosan-PRP with wrapping was partially healed (c, d). There was no repair tissue in the group treated with wrapping only (e, f). In the two cases where repair was observed (a to d), the repair tissue was highly cellular, well integrated to the adjacent meniscal tissue, but structurally different than the intact contralateral menisci (g, h). Significant cell recruitment to the outer portion of all treated menisci was observed (a, c & e) compared to intact contralateral menisci (g). Suture tracks were frequently observed in menisci treated with the wrapping technique (c & e). Rectangles in panels a, c, e & g demonstrate regions where the higher magnification images b, d, f & h were acquired.