

An Experimental Study of Vascular versus Minimal Vascular Microenvironment to Induce Cartilage Healing

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Introduction

The microenvironment in the cartilage defect might be a key factor in order to achieve a functional repair tissue. The influence of bonemarrow as a source of repair cells and growth factors concerning cartilage repair is not well documented.

Aims

This long- term experimental study evaluates the effects of the cartilage defect as a bioactive chamber with and without access to the bone marrow.

Methods

In thirtyfive New Zealand rabbits 22 weeks of age, a defect was induced in patella of both knees at time zero. Additionally one control sham-group of 6 rabbits served as baseline for the experimental results. After 2 weeks the defects were repaired. Thirty-six weeks after the repair the animals were sacrificed and the repair tissue evaluated. Preoperatively at each of the three time points a wash out sample from the joint was collected by installing 2cc NaCl into the joint, doing 50 cycles of full ROM before the sample was aspirated. The surgical procedure included a bilateral arthrotomy using a biopsipunch ($\phi = 4$ mm) to induce the cartilage lesion. Microsurgery instruments and a Zeiss stereomicroscope were used to secure removal of all the cartilage tissue in the defect down to the subchondral bone plate. At the rearthrotomy two weeks later, one of the knees was randomized to have 4 drill holes ($\phi = 0,6$ mm) drilled by hand in the defect to make access to the subchondral bone marrow, thus creating a vascular chamber. The defect in the other knee remained minimal vascular. A periosteum flap was harvested from the anteriomedial part of tibia and placed at the defect with the cambium layer facing down and sutured with four 9.0 sutures to the edge of the defect and glued with Tissel glue®. All rabbits were observed for one week in their cages while antibiotics and analgesics were administered. After one week the rabbits were allowed to move freely on a 10-m² floor. Synovial fluid was analyzed proteoglycan concentration using standard ELISA technique. In the control-sham group the control joint were left untouched while the sham-joint were exposed for air in 20 minutes at time zero and at time point two weeks. Sacrifice were done after 1,2 and 36 weeks after repair of the cartilage defect

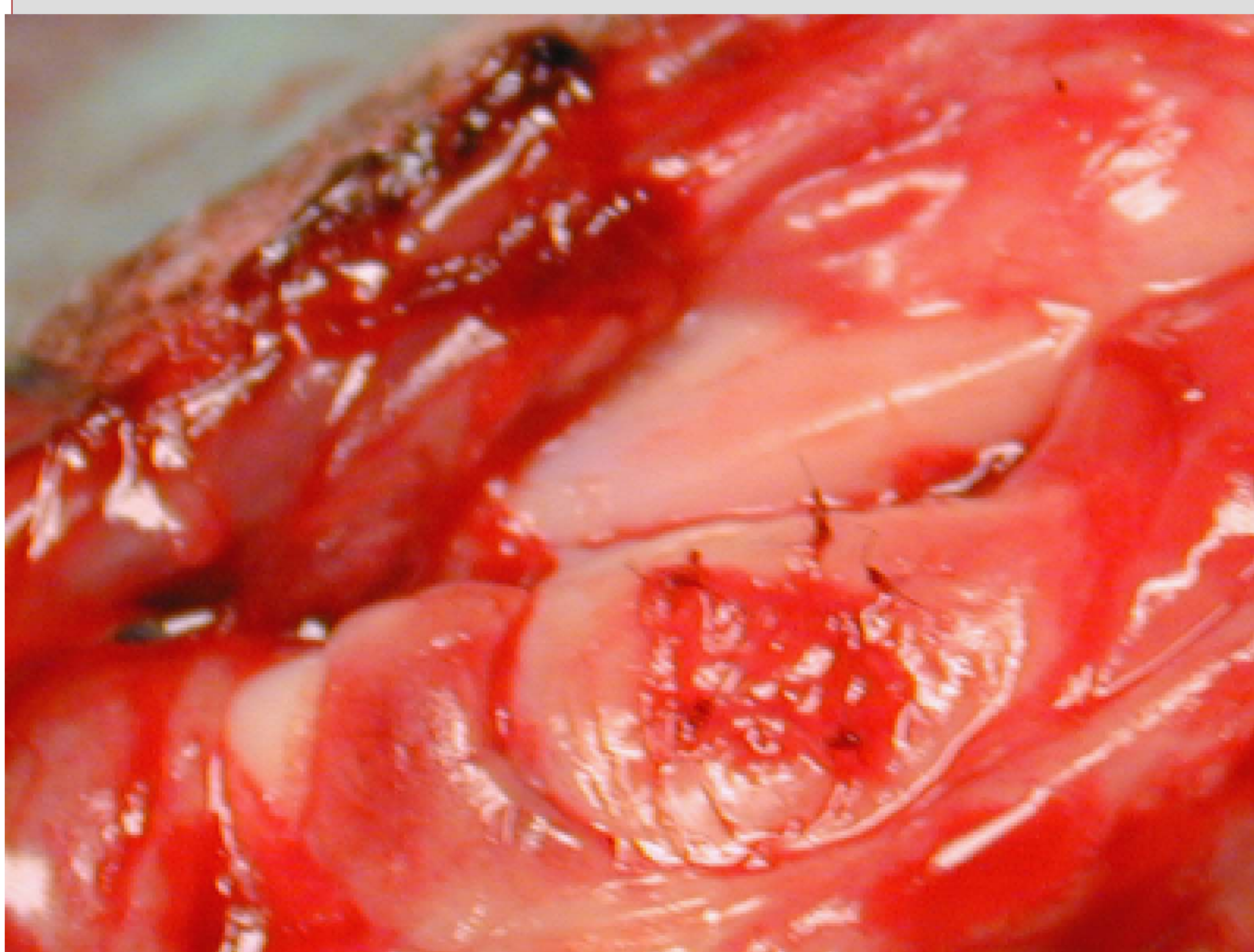


Figure 1. Sticked (9.0) fixed the the periosteal flap to the edge of the cartilage defect and Tissel glue was used to cover the transplanted graft.

Results

Macroscopically a soft gelatinous repair tissue was observed in all experimental defects though none were completely filled. Histological the repair tissue was classified as fibrous tissue. Penetration and access to patellar bone marrow was observed in all samples of the vascular procedure. The proteoglycan analyses showed a slight increase in both groups at two weeks but returned to the preexperimental level at sacrifice (age 60 weeks). All knees showed full range of motion and macroscopically no degenerative changes were noted. The vascular side showed a percentage of filling of 50 % \pm 6 % while the minimal vascular side was evaluated to 33 % \pm 6 %, $p = 0,011$. Interface binding of the repair tissue to the subchondral bone was 62 % \pm 9 % at the vascular side and 41 % \pm 26 % at the minimal vascular side, $p = 0,33$. Height of the cartilage tissue in the center of the defect were significantly lower $p = 0,0030$ than the control-sham group and no significant difference could be found between the minimal vascular group and vascular group $p = 0,72$. Further histomorphometry measurements demonstrated reduced cartilage rim and also degenerative changes including loss of chondrocytes and erosion at the surface of patella cartilage. Additionally the vascular experimental group revealed significantly increased thickness of the subchondral bone plate both at two weeks and at 36 weeks after repair $p = 0,021$.

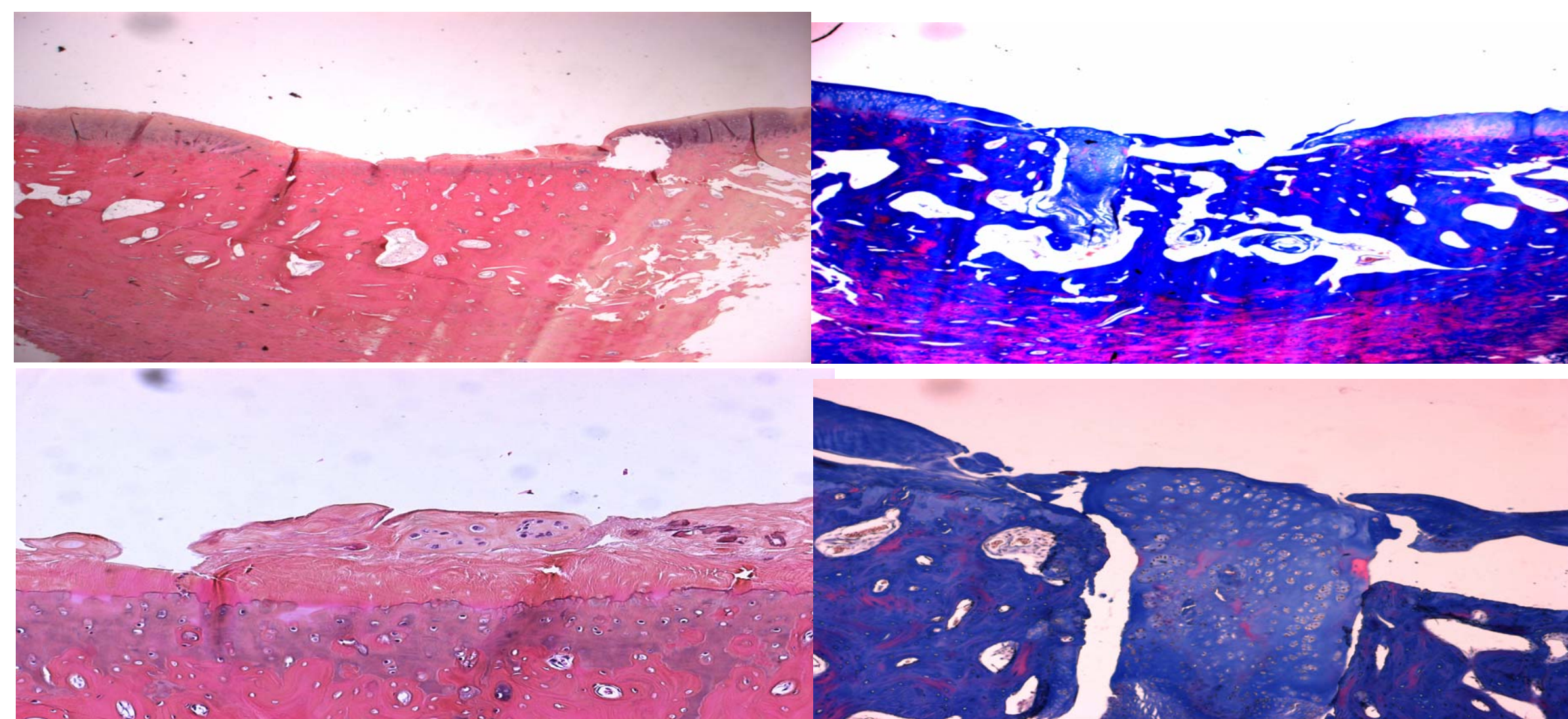


Figure 3. Histological appearance of the defects at 36 weeks. At the left side a typical view of the minimal vascular side and a higher magnification showing the fibrous tissue found in the defect. At the right side a vascular defect are shown with magnification of the microfracture "plugg" in the defect.

Filling of Cartilage Defect Area

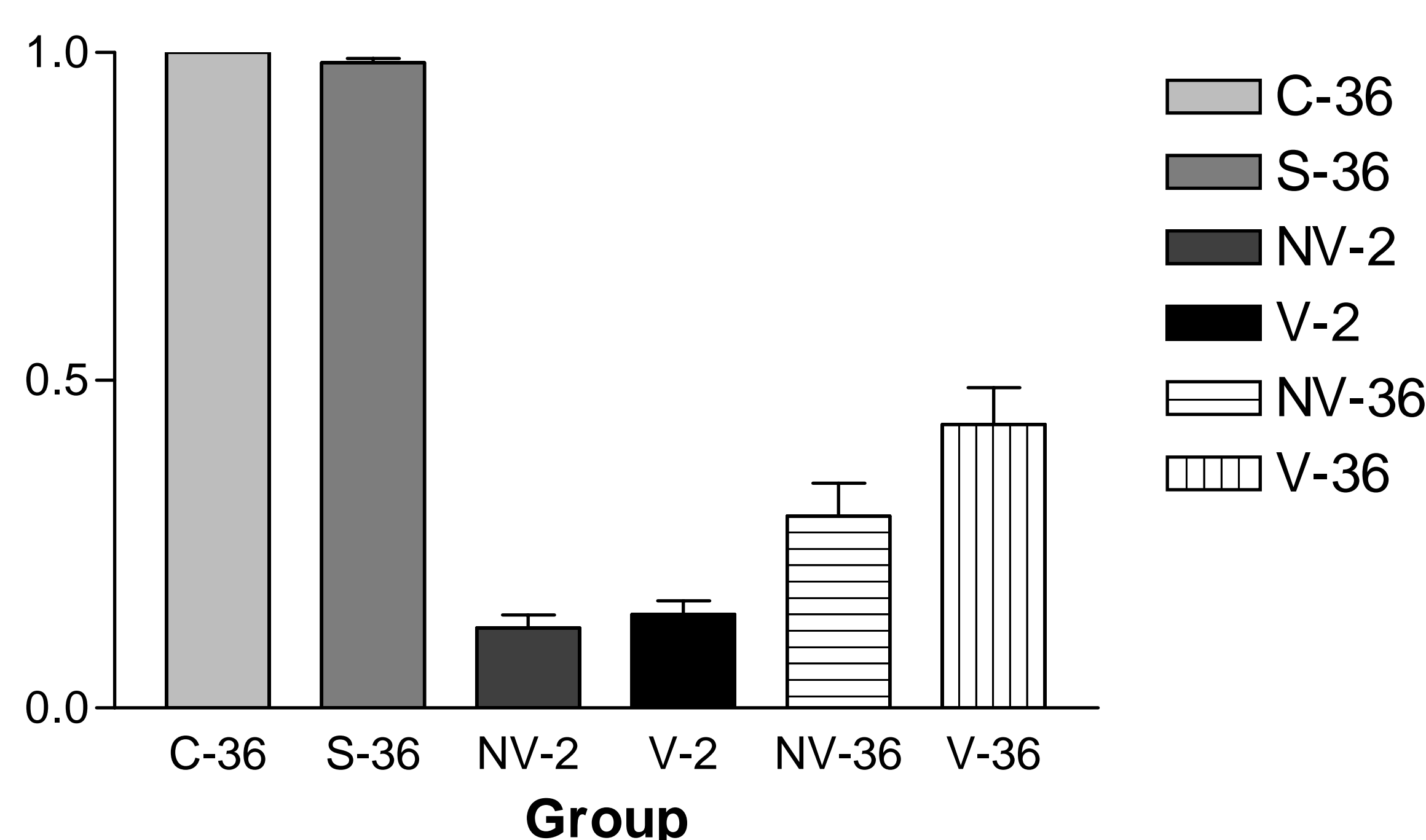


Figure 3. Histogram of the filling of the defect at the different time points. Highest filling was observed in the vascular experimental group at 36 weeks.

Group	No	Mean filling % of defect	Subchondral bone % binding and thickness		Cartilage μ m	
			Center	Rim	Center	Rim
Control	7	98 \pm 1	98 \pm 1	622 \pm 23	652 \pm 27	495 \pm 37
Sham	7	98 \pm 1	92 \pm 7	652 \pm 59	805 \pm 35	555 \pm 48
MV-1 w	6	30 \pm 8	12 \pm 9	534 \pm 86	156 \pm 43	398 \pm 43
V-1 w	6	40 \pm 9	24 \pm 10	580 \pm 93	288 \pm 87	356 \pm 17
MV-2 w	12	14 \pm 3	34 \pm 12	540 \pm 22	26 \pm 8	336 \pm 24
V-2 w	12	16 \pm 2	46 \pm 11	706 \pm 44	49 \pm 16	366 \pm 26
MV-36 w	16	33 \pm 6	41 \pm 9	544 \pm 34	175 \pm 57	333 \pm 48
V-36 w	16	50 \pm 6	62 \pm 7	687 \pm 67	225 \pm 41	351 \pm 34

Table 1: Histomorphometry measured parameters presented as mean \pm SE



Figure 4. Macroscopic view of the defect after an observation period of 36 weeks. A = vascular microenvironment, B = Minimal vascular microenvironment.

Discussion

Previously an minimal vascular chamber using periosteum as a membrane has been investigated and similar results has been found (1). This study shows that such a bioactive chamber supplied with bone marrow elements provided through minor penetration of the subchondral bone plate is not sufficient to restore a functional cartilage tissue.

Conclusions

Both experimental groups using a rim sutured periosteal flap showed a incomplete repair consisted of fibrous scar tissue, but the degree of filling was greater in the vascular microenvironment. The failed repair with incomplete filling was accompanied by structural changes indicative of a degenerative process in the defect and the adjacent cartilage

References

1. Brittberg M, Nilsson A, Lindahl A, Ohlsson C, Peterson L: Rabbit articular cartilage defects treated with autologous cultured chondrocytes. *Clin Orthop* : 270-283., 1996

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