

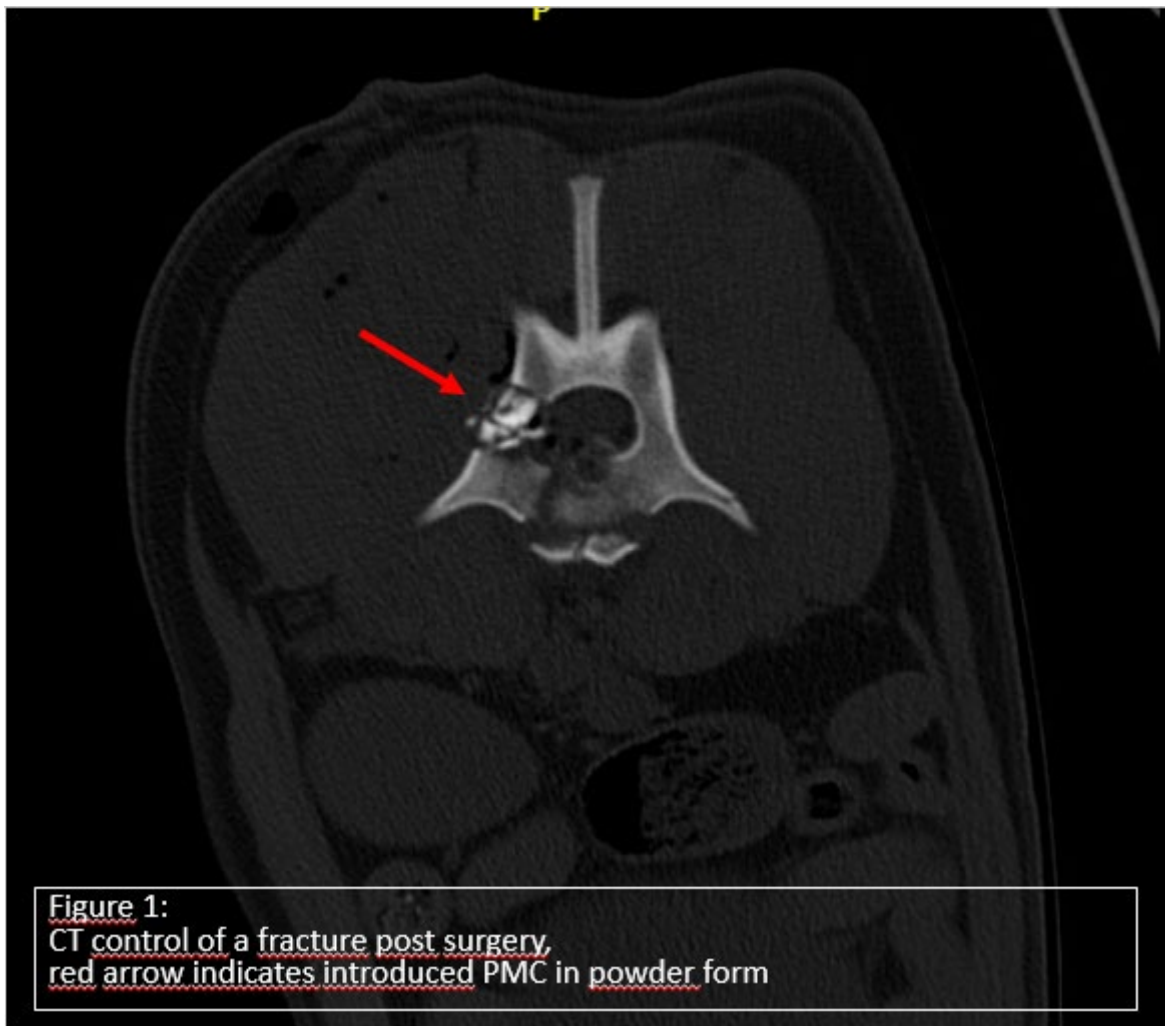
Albert- Heim- Stiftung

Interim Report

Project Title:	Surgical cervical intervertebral bony fusion with PMC in dogs after ventral slot surgery
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Reporting Period:	January 2021- February 2023
Project Summary:	After spinal surgery associated with disc removal there is an incomplete bone fusion between vertebrae, even after implant application for stabilisation. This is a well-known problem both in humans and in animals. A resorbable ceramic material with intrinsic osteoinductivity, that drives formation of bone, has been developed (PMC). After implantation of this material into a bone defect, it results in formation of new bone tissue and resorption of the implanted ceramic material. A pilot study including four mini pigs was performed. The osteoinductive material was implanted between cervical vertebrae after a ventral slot was performed and serial control CT scans were performed. The last CT scans were performed 12 months after surgery. All CT scans show the expected results (bone fusion). All mini pigs were doing very well clinically. Our project aims to use the developed ceramic material in a clinical setting in dogs to allow technology transfer to promote bone healing to other species (humans, horses, ruminants). Privately owned dogs with spontaneous disc disease, vertebral fractures or other cervical conditions subjected to surgery, will be included in the study (30 dogs in the PMC group and 20 dogs in the control group). The ceramic material will be placed in the surgically created slot between the cervical vertebrae, and the fate of the implant and its bone forming capacity will be investigated using serial follow-up diagnostic imaging.

Activities and Current Progress:	The animal experimentation permit (BE18/21) was obtained. A pilot dog with caudal cervical spondylomyelopathy was operated. The nine year old Weimeraner showed generalized ataxia and tetrapareses. Distraction and stabilization at C5/C6 with plate and screws was performed and PMC was introduced into the space of the discectomy at C5/C6. Additionally ventral fenestration at C6/C7 was carried out. A control CT scan was performed after surgery, which showed the correct alignment of vertebrae. Additionally three cases of atlantoaxial instability were surgically stabilized and the PMC was introduced. One vertebral fracture was treated with introduction of PMC as well. During the surgery the application of the PMC was more difficult than expected. Precise application of the powder form was difficult but the control CTs, performed after surgery, showed a correct position of the PMC implant in all cases (example of vertebral fracture in figure 1). After surgery, the pilot dog with cervical spondylomyelopathy was in good general condition with only very mild residual neurological symptoms. Several weeks after surgery the dog showed neck pain, so a control was carried out earlier than planned. The neurological signs worsened compared to the examination directly after surgery. Unfortunately, implant failure was detected and all implants (plate, screws, PMC) had to be removed. Even though the operated case was a difficult surgical case with a guarded prognosis, the implant failure necessitated an improvement of the PMC. Additionally the difficult application of the powder form led to the need to adjust the PMC. After various discussions and agreements with our partners at Uppsala University, a process to improve the PMC was set in motion and finally carried out by the responsible department of Uppsala University. Changing the form of the implant required a safety study that has been performed between July and November 2021. Due to the COVID situation one component of the new foreseen matrix had some delay in delivery. In conclusion, the powder form was changed to a self-hardening paste form. During this process we decided to not operate other dogs until we improved the material. The first eight dogs were operated with the new paste- like PMC material. Post surgery CT controls showed correct application of the PMC paste in the region of the bone defect. Several T1 (three months post surgery) and T2 (six months post surgery) controls were performed of the upper mentioned eight dogs operated. On the control images it is seen, that the material moved slightly towards ventral into the adjacent paraspinal musculature (figure 3), where bone formation and integration can be seen within the paraspinal muscles (figure 4).
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	The findings are consistent with the impression during the surgeries, where the new paste appeared somewhat too liquid, making application slightly difficult. Even if the too liquid material does not show the expected clear bone formation within the bone defect because of the ventral movement out of the defect, important knowledge could still be gained. Bone formation functions in the area of the muscles. This is an integral and important part of the success of bone fusion as achievement of osteogenesis in soft tissues like muscles is considered more difficult than in bony environment. Currently the material again is being modified by our partners at Uppsala University to gain a slightly more solid texture with the goal that the material rests completely in the bone defect and can fully develop its osteogenic capacities within the defect. Additionally some dogs were included in the control group. Furthermore, from my personal side my maternity leave, the reduction in employment percentages due to childcare and my preparation time for the board exam also slowed down the expected progression of the study.
Future Prospect:	Due mainly to the setback of difficult application, not satisfactory consistency of PMC and therefore the need to modify the PMC twice, our planned case load is lacking behind expectations. We are confident, that the performed modification of PMC will solve the problem of the too liquid texture and difficult application during surgery. With a second mutation of the ceramic material we are convinced, that we will see the expected improved bone proliferation within the defect on the control CT scans. Currently we are awaiting the new textured PMC until operating other dogs. Additionally further studies with other regions of difficult or prolonged bone healing are planned as soon as the material is modified.



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