



**Karolinska  
Institutet**

Institutionen för Molekylär Medicin och Kirurgi.

# **Development of Surgical Techniques in Craniofacial Reconstruction**

Akademisk avhandling

som för avläggande av medicine doktorsexamen vid Karolinska Institutet offentligen försvaras i  
ÖNH:s föreläsningssal (A6:02), Karolinska Universitetssjukhuset, Solna

Fredagen den 25:e november 2016 kl. 09.00

av

**Erik Neovius**

*Huvudhandledare:*

Filip Farnebo  
Karolinska Institutet  
Institutionen för Molekylär Medicin och Kirurgi

*Bihandledare:*

Thomas Engstrand  
Karolinska Institutet  
Institutionen för Molekylär Medicin och Kirurgi

Kalle Lundgren  
Karolinska Institutet  
Institutionen för Molekylär Medicin och Kirurgi

*Fakultetsopponent:*

Avni Abdiu  
Linköpings Universitet  
Institutionen för Klinisk och Experimentell Medicin

*Betygsnämnd:*

Ann Hermansson  
Lunds Universitet  
Institutionen för Kliniska Vetenskaper

Bodil Lund  
Karolinska Institutet  
Institutionen för Odontologi

Paul Ackermann  
Karolinska Institutet  
Institutionen för Molekylär Medicin och Kirurgi

# ABSTRACT

*Introduction:* Facial fractures are common and either the injury or the surgical treatment may cause sequelae including diplopia, visual loss, dystopia, enophthalmos, scarring, soft tissue affection and sensory disturbances. Severe facial fractures may also lead to bone defects due to resorption. In bone reconstruction after facial fractures, tumor surgery or anomalies, replacement using autologous bone is the gold standard treatment. However, in order to avoid donor-site morbidity and risks, reduce surgery time and hospital stay; the interest in artificial bone substitutes is increasing.

The aim with these studies was to better understand risks and complications related to craniofacial surgery and thereby improve surgical treatment. Additionally, to explore bone substitutes in order to avoid donor site morbidity.

*Methods:* In study I-II patients with facial fractures were grouped based on the severity and location of injury and examined three years or more after surgery regarding vision, diplopia, dystopia, enophthalmos and infraorbital nerve (ION) sensibility. Study III included patients treated for a facial fracture including lower eyelid incisions. The outcome after subciliary and transconjunctival incisions with regards to the long-term occurrence of ectropion, scleral show, entropion and canthal malposition was examined. Study IV was a prospective randomized study comparing the healing capacity between BMP-2 (250 µg/ml) in hydrogel, hydrogel without BMP-2, Spongostan™ (negative control) or Tisseel™ with autologous bone matrix (positive control) in critical size cranial bone defects in neurosurgery. Study V was a prospective randomized study investigating the healing capacity of BMP-2 (50 µg/ml or 250 µg/ml) in hydrogel compared to treatment with autologous bone in alveolar cleft surgery.

*Results:* In Study I and II, 81 patients attended to follow-up. Diplopia occurred in 3.7%, visual loss in 2.5%, dystopia in 4.9% and visible enophthalmos (>2 mm) in 8.6% (Study I). Severe diplopia was found in two patients (2.5%) and was due to nerve injuries, the trochlear and abducens nerve respectively. Complex fractures had a higher incidence of any sequelae. In Study II we found affected ION sensibility in 20% and severely affected sensibility in 7.4% but there was no statistically significant correlation between questionnaire results and log von Frey values. In Study III, including 128 patients, 8.1% had ectropion and 11% had scleral show in the subciliary group whereas 2.2% had ectropion, 4.4% had scleral show and 2.2% had a canthal malposition in the transconjunctival group. This difference was not statistically significant.

In Study IV we found that Tisseel™ with autograft, hydrogel and hydrogel with BMP-2 had a significantly better bone healing capacity than negative controls (Spongostan™). Frontal bone originating from the neural crest had significantly better bone healing than parietal/temporal bone originating from the mesoderm. In Study V the bone healing capacity was comparable between BMP-2 (250 µg/ml) in hydrogel and autologous bone graft from the iliac crest after six months. Severe gingival swelling was noted in patients treated with BMP-2 (250 µg/ml) in hydrogel and therefore the study was prematurely closed.

*Conclusions:* Diplopia after facial fractures may be caused by ocular motor nerve injuries, not only by hinged eye muscles, fibrosis or malposition of the eye, which emphasizes the importance of meticulous eye examinations in trauma patients. For access to the orbit transconjunctival lower eyelid incisions had a lower risk for ectropion and scleral show compared to subciliary incisions. von Frey monofilament assessment does not fully correlate with all aspects of sensory disturbance of the ION after facial fractures.

Due to insufficient bone healing capacity in cranial bone defects in adults (partial thin bone healing) and severe adverse events in alveolar cleft surgery in children (gingival swelling), we dissuade treatment with BMP-2 in craniofacial bone reconstruction.