Title: Occipitocervical instrumented fixation utilising patient-specific C2 3D-printed spinal screw trajectory guides in complex paediatric skeletal dysplasia.

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1. **Abstract:**

**Purpose:**

Instability of the craniocervical junction in paediatric patients with skeletal dysplasia poses a unique set of challenges including anatomical abnormalities, poor bone quality, skeletal immaturity and associated general anaesthetic risks. Instrumented fixation provides optimal stabilisation and fusion rates. The small vertebrae make the placement of C2 pedicle screws technically demanding with low margins of error between the spinal canal and the vertebral artery.

**Methods:**

We describe a novel clinical strategy utilising 3D-printed spinal screw trajectory guides (3D-SSTG) for individually planned C2 pedicle and laminar screws. The technique is based on a pre-operative CT scan and does not require intraoperative CT imaging. This reduces the radiation burden to the patient and forgoes the associated time and cost. The time for model generation and sterilisation was <24 hours.

**Results:**

We describe two patients (3 and 6 years old) requiring occipito-cervical instrumented fixation for cervical myelopathy secondary to Morquio syndrome with 3D-SSTGs. In the second case, bilateral laminar screw trajectories were also incorporated into the same guide due to the presence of high-riding vertebral arteries. Registration of the postoperative CT to the pre-operative imaging revealed that screws were optimally placed and accurately followed the predefined trajectory.

**Conclusion:**

To our knowledge, we present the first clinical report of 3D printed spinal screw trajectory guides at the craniocervical junction in paediatric patients with skeletal dysplasia. The novel combination of multiple trajectories within the same guide provides the intraoperative flexibility of potential bail-out options. Future studies will better define the potential of this technology to optimise personalised non-standard screw trajectories.
2. Introduction:

Morquio A syndrome (MPS IV) is an autosomal recessive lysosomal storage disorder characterised by short stature and diffuse skeletal abnormalities[1]. Patients frequently present in the first decade of life with progressive myelopathy secondary to craniocervical instability[2], this has led some authors to recommend prophylactic occipito-cervical fusion[3]. However, MPS IV patients present significant anaesthetic and surgical challenges due to factors such as short stature, respiratory compromise, poor bone quality and skeletal immaturity.

Instrumented fixation is the gold standard to achieve effective and durable treatment of atlantoaxial instability in this patient group. A long-term outcome study revealed that instrumented fixation resulted in fusion in up to 95% of patients, but delayed adjacent level instability was seen in up to 35% at a mean of 7 years following the initial procedure[4]. Recognised techniques include occipito-cervical fixation (OC), C1-2 fixation through C1 lateral mass-C2 pars or pedicle screw constructs (Harms-Goel procedure[5, 6]), C2 laminar screw constructs[7], and C1-2 transarticular screw placement (Magerl procedure[8]). In MPS IV patients the combination of young age at the time of surgery, small bone size and intrinsic bone dysplasia increase the risks of neurovascular injury and construct failure forcing surgeons to use semirigid fixation techniques instead[9].

Semirigid techniques comprise sublaminar and interspinous wiring techniques such as Brooks[10], Gallie and Sonntag methods in which interposition bone grafts are held in place with steel wires to promote posterior fusion[11]. Semi-rigid techniques are biomechanically inferior to instrumentation and so wiring techniques are mostly employed as adjunctive measures[12] or salvage techniques when instrumented fixation methods are deemed not possible, have failed or carry too high a risk due to the unfavourable bony anatomy[13]. Furthermore, external orthoses, such as Halo-body jackets are frequently required following semirigid techniques which present additional challenges[14] and are unacceptable to patients and families.

Three-dimensional (3D)-printed spinal screw trajectory guides (3D-SSTG) have been described to aid with pedicle screw fixation. Meta-analyses of randomised control trials[15], almost exclusively focusing on thoracic and lumbar pedicle screw placement in adolescents and adults, have shown improved placement accuracy rates[16], reduced intraoperative radiation exposure[17] and decreased operative times with these devices compared to freehand screw placement. For craniocervical fixation, guides are custom-made medical devices that conform to the lamina and spinous process of the C2 vertebra derived from the pre-operative CT scan. A handle allows the surgeon or assistant to maintain contact with the bone whilst the drill bit and manufacturers drill guide are placed within extruded cylinders arising from the guide[18]. This allows the predefined trajectory to be safely drilled to the desired depth.

To date, 3D-SSTG for use at the CVJ has not been described in children with Morquio syndrome. Optimised screw placement and reduced radiation exposure associated with intraoperative CT would offer significant advantages in the pediatric population with congenital craniovertebral anomalies.

We present two cases in which a 3D-SSTG has been used to facilitate safe occipito-cervical fusion with bilateral C2 pedicle screw placement in the first case and bilateral C2 laminar screw placement in the second. The second case was particularly novel as the 3D-SSTG incorporated two trajectories within the same guide giving the surgeon the flexibility to decide intraoperatively and potentially combine different trajectories based on lateralised anatomical variations.
3. Methods:

Two paediatric patients with Morquio A syndrome undergoing occipito-cervical instrumented fixation for cervical myelopathy secondary to craniocervical instability between November and December 2020 are the subject of this report.

Model generation: 3D-SSTG Design and build. Bony segmentation was performed from the pre-operative CT scan of the cervical spine (voxel resolution 0.70×0.70×0.70 mm) performed within the preceding 3 months of the surgery utilising the Materialise Mimics Base 18.00 software (Materialise NV, Technologielaan 15, 3001 Leuven, Belgium). A 3D spinal reconstruction (Figure 1) was generated from the DICOM volume and 3.5 mm cylinders were used to simulate the screw trajectories (Figure 2). A negative contact surface to that of the spinous process and laminar were generated using the Mimics 3-Matic software (Materialise NV, Technologielaan 15, 3001 Leuven, Belgium) as previously described by Feng et al [19]. The screw trajectories were optimised to maximise distance from the spinal cord and vertebral artery on each side independently. The entry and exit points of the screws on the surface of the 3D reconstruction were then used to create extrusions (radius 3 mm) from the centre point of the trajectory to match the outer diameter of the drill guide with a 0.2 mm tolerance (diameter 6 mm). The extruded drill guide components and a handle were then connected to the negative spino-laminar surface through a Boolean union (Figures 2). The 3D-SSTGs were printed in ‘Surgical Guide resin’ on the FormLabs 3B (Formlabs Inc. Somerville, MA) biomedical printer. The models were then washed in 99% ethanol before UV curing and removal of support structures. Sterilisation was then undertaken following the manufacturers recommended autoclave sterilisation protocol of 3 minutes at 138 °C.

Surgical procedure: Patients were operated on using a total intravenous anaesthetic (TIVA) technique to facilitate the use of MEP and SSEP. Baseline potentials were established before positioning. Patients were positioned prone on a paediatric Montreal mattress with heads secured in a Mayfield clamp. Lateral fluoroscopy was used to optimise craniocervical reduction. A midline suboccipital exposure from inion to C3 was performed followed by C1 laminectomy. Instrumented fixation was performed in both cases utilising the MOUNTAINEER® Occipito-Cervico-Thoracic Spinal System (DePuy Spine, Inc. Raynham, MA). A contoured occipital plate was first screwed to the occiput followed by placement of the 3D-SSTG on the posterior aspect of the exposed C2 vertebra. The manufactures drill guide with pre-set depth stop was subsequently placed within the 3D-SSTG and the trajectory was drilled utilising a handheld electric drill. A probe was then placed within the drill hole and all margins were palpated to confirm no cortical breach. The probe was then left in place and the contralateral trajectory was drilled in the same fashion. The drill guide was then removed and the screws were placed along the pre-drilled trajectories. The screw and occipital plates were finally connected by contoured rods bilaterally. The surrounding bone was decorticated and bone graft was placed to aid fusion (Figure 4). Low dose CT scans were performed before discharge to ascertain screw placement, bony alignment and extent of decompression (Figure 5). The pre- and post-operative CT scans were registered to common space and the instrumentation were segmented to show their relative position compared to the pre-planned trajectory and guide. Implanted screw trajectories were <0.7 mm of the intended planned trajectory, which is less than the error associated with measurement.

Results

Patients: Case 1
A three-year-old boy with Morquio A syndrome presented with progressive myelopathy affecting the upper and lower limbs. The pre-operative CT scan of the cervical spine is shown in Figure 1 revealing severe cervical stenosis and severe instability. The 3D reconstruction of C1-3 revealed the extent of the anteriorlisthesis of C1 whilst the axial and coronal images reveal the presence of rotational and coronal plane deformities respectively. The MRI scan (not shown) revealed severe compression at the level of C1 with increased T2 signal intensity within the spinal cord. The planned trajectories and corresponding 3D printed guide and 3D vertebral model are shown in Figure 2A-C. The duration of surgery was 2 hours 20 minutes. The boy made an uneventful recovery from surgery and was discharged from hospital on postoperative day 4.

Case 2:

Six-year-old girl with Morquio A syndrome presented with mild quadriaparesis, she was independently mobile in the home environment but wheelchair dependent outdoors. MRI, shown in Figure 3, demonstrated flattening of the spinal cord at C1 with intramedullary signal changes on T2 weighted imaging. The planned trajectories and corresponding 3D printed guide and 3D vertebral model are shown in Figure 2D-F. The duration of the surgery was 1 hour 30 minutes. She made an uncomplicated recovery from surgery and was discharged from the hospital on postoperative day 4.

The intraoperative use of the drill guides for both cases is shown in Figure 4 and the postoperative CT scans with registration to the pre-operative CT and overlay of the 3D-printed guide shown in Figure 5.

At 5 months following surgery neither patient developed any infection or wound related complication.

4. Discussion:

Case series of Morquio disease reveal that the mean age at the time of surgery is around 4 years.

In addition to the cervical instability, chest wall deformity, airway obstruction and predisposition to lower respiratory infections add to the complexity of general anaesthesia[1]. Shorter operative times are therefore preferable to minimise the risk of anaesthetic related complications.

Biomechanical studies have shown that instrumented fixation is preferable to sublaminar wiring, where possible, and constructs connecting to C2 pedicle screws have similar strengths to C2 laminar screws[20]. Furthermore, C2 laminar screw constructs appear to provide greater stabilisation against rotatory movements[21]. The combination of a short neck, high riding vertebral arteries and short pedicle heights make C2 pedicle screw placement challenging or impossible if the pedicle height is less than the diameter of the screw used (typically 3.5 mm). The biomechanical force of occipital fixation terminating at the C2 screw is significant and carries a risk of screw failure or pedicle fracture especially if the bone quality is poor. To mitigate this, some authors extend the construct to below C2 whilst others have described placing both laminar and pedicle screws at the same time, termed ‘C2 hybrid screws’[22]. Occipital fixation is indicated where C1 laminectomy is required, where there is a degree of instability between C1 and the occiput due to ligamentous laxity or when the C1 vertebra is inadequate for fixation. This is a common occurrence in children with Morquio A syndrome.

3D-printed drill guides have been described for spinal screw fixation. A recent meta-analysis comprising seven randomised control trials and six prospective cohort studies have shown that 3D printed guides are superior to free-hand pedicle screw placement in terms of accuracy and shorter operative time[15]. Pooled data revealed optimal screw placement was almost 3-fold more likely
with 3D-printed drill guides compared to freehand placement (OR = 2.88 95% CI = 2.39-3.47).

Furthermore, studies have also shown 3D printed guides to be non-inferior to navigation and robot-assisted spinal screw placement. Additionally, in contrast to the latter two techniques 3D printed guides do not require a large capital outlay, forego the need for an intraoperative registration scan, thus preventing excess radiation exposure and reduce comparative operative time even further. Studies focusing particularly on spinal deformity have shown an even greater comparative benefit with 3D-printed drill guides over freehand pedicle screw placement[23].

Most applications of 3D-SSTGs have largely focused on thoraco-lumbar pedicle screw placement in adults. The major differences being: 1) the size of the pedicles and hence the error tolerance, 2) the extent of bony exposure and by implication the surface area for bone-guide contact and 3) the proximity to critical neurovascular structures. High cervical pedicle screws mandate a very low margin for error. Medial breaches may compromise the spinal cord resulting in severe neurological sequelae, inferio-lateral breaches may result in damage to the V2 segment of the vertebral artery and C3 nerve root, direct lateral breaches may damage the V3 segment of the vertebral artery and result in poor mechanical stability whilst superior breaches may compromise the C2 nerve root. The standard anatomical structures that require exposure for thoracolumbar pedicle screw guides include the pars interarticularis, the facet complex and the transverse process. The surface area for contact varies between different 3D-SSTG designs but the larger thoracic and lumbar vertebrae afford greater bone-guide conformity and hence increased stability with less chance of slippage or inaccurate guide contact during drilling. Greater bony exposure is easier to achieve in the thoracolumbar spine but is significantly limited in the high cervical spine. For C2 screw placement contact is principally limited to the lamina. The bifid nature of the spinous process and corresponding overhang created by this in relation to the proximal spinous process makes guide conformity in this area hard to achieve. Furthermore, proximity of the vertebral artery lateral to the C2 pars interarticularis makes lateral bony exposure risky.

We present two paediatric cases of Morquio A syndrome with craniocervical instability and spinal cord compression. In both cases, instrumented fixation was a significant challenge due to the extent of skeletal dysplasia and proximity to critical neurovascular structures. 3D-SSTG for C2 screws is a novel alternative application that allows the optimal screw trajectory to be planned pre-operatively and applied easily during surgery reducing both the radiation burden from intraoperative fluoroscopy as well as overall operative time.

The presented technique can be seamlessly integrated into the surgical workflow requiring 24 hours of notice before surgery. The surgical models required 3 hours of printing time with the FormLabs 3B biomedical printer. The subsequent washing, curing and removal of support structures from the model took an additional one hour. The models are then sent for sterilisation overnight in time for surgery the following morning. The 3D-SSTGs were presented to the surgeon with a sterilised model of the vertebra so that the exact fit of the guide to the vertebra intraoperatively could be determined. The main limitation of 3D-SSTGs is the potential for incorrect placement of the guide on the vertebra. To mitigate this, the 3D-SSTGs were labelled with left and right laterality as well as the vertebral level (C2). Also, the conformity of the 3D-SSTG to the vertebra is exact and care is needed during the muscle dissection to prevent any excess soft tissue from preventing adequate contact. For this reason, the models are manufactures using a semi-transparent resin and the entire contact surface can be visualised for any incongruity. Additionally, due to the follow-up duration we are unable to report on the fusion rate associated with this technique. Despite this, there is no reason to believe that the use of a 3D-SSTG to aid screw placement would affect the fusion rate compared to other case series performing occiput-C2 fixations without a 3D-SSTG.
5. Conclusion:

To our knowledge, this is the first report of the application of 3D-SSTGs at the craniocervical junction in cases of paediatric Morquio A syndrome and the novel introduction of multiple trajectories within the same guide to provide the surgeon with the flexibility to change, or even combine, the screw trajectories during the procedure. The pre-planned nature of the trajectories also opens the potential for automated trajectory algorithms to plan safe trajectories that maximise distance from neural and vascular structures whilst ensuring the threads of the screws are within the greatest density bone based on the Hounsfield units of the CT scan. Morphological analysis from increased numbers of patients would allow the creation of a group atlas and help to identify particular anatomical abnormalities of C2 in this group of skeletal dysplasia. This could open the possibility of non-standard personalised screw trajectories that are biomechanically optimised for that specific patient and pathology. Further work will concentrate on incorporating multiple trajectories within a single guide and on the validation of automated trajectory algorithms, as these can now be placed with confidence using 3D-SSTGs or even robotic assistance. The long-term outcomes regarding fusion rates are also awaited.

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References:


Figure 1: Pre-operative CT scan with 3D reconstruction from Case 1

Figure 1 Legend: (A) Axial, (B) Sagittal, (C) Coronal and (D) 3D reconstruction of the cervical vertebra. The axial and sagittal images (A and B) reveal significant spinal stenosis at the atlanto-axial level with odontoid hypoplasia and increased atlanto-dental interval. Arrows depict the deformity secondary to anterolisthesis of C1.

Figure 2: Trajectory planning

Figure 2 Legend: 3D reconstruction of C2 from Case 1 from posterior (A) and lateral (B) views depicting planned C2 pedicle screw trajectories to maximise distance from the spinal cord and high riding vertebral artery. Yellow cylinders represent the 3.5 mm diameter screw trajectories from which the spinal screw trajectory guide (C) is derived. The corresponding C2 vertebral model was also 3D printed for pre-operative safety checks and during intraoperative use. 3D reconstruction of C2-4 from Case 2 from superior (D) and lateral (E) views depicting the planned C2 pedicle (yellow) and laminar (red) screw trajectories to maximise distance from the spinal cord and the high riding vertebral artery. Due to the high riding vertebral artery, there was no potential to place a 3.5 mm diameter screw without breaching into the vertebral foramen or breaching the superior aspect of the pars. The angulation of the C1/2 lateral mass joint was also unfavourable and would likely result in the drill breaching the cortical surface. A laminar screw trajectory was consequently incorporated into the same trajectory guide (C). The trajectories of the laminar screws are angled in the craniocaudal direction so that the screw heads do not clash and so that the polyaxial screws can be connected to the rods easily.

Figure 3: Pre-operative MRI scan with 3D reconstruction from Case 2

Figure 3 Legend: (A) Sagittal T2 MRI and B) 3D reconstruction of the cervical vertebra. The sagittal image (A) reveals significant spinal stenosis at the C1 level causing spinal cord compression. The 3D reconstruction reveals a short pedicle (3 mm in the craniocaudal dimension) due to high riding vertebral arteries bilaterally and odontoid hypoplasia.

Figure 4: Intra-operative use of drill guides

Figure 4 Legend: Intraoperative images revealing placement of the 3D printed spinal screw trajectory guide placed on the back of the C2 vertebra for Case 1 (A) abd 2 (C). The occipital plate and C1 laminectomy had already been performed. Final image after insertion of the laminar screws and connection to the occipital plate through rods bilaterally (B and D).

Figure 5: Post-operative CT scans and 3D reconstructions of instrumented constructs:
Figure 5 Legend: Orthogonal axis through the screw trajectories of the right (A) and left (B) sided C2 pedicle screws from Case 1 and right (D) and left (E) sided C2 laminar screw from Case 2 with in-plane 3D reconstructions of the instrumented constructs (gold). Co-registration of the pre- and post-operative CT scans allows the position of the instrumented constructs (gold) to be seen in relation to the pre-operatively designed guide for Case 1 (C) and the pre-planned trajectories for Case 2 (F). In (F) the C2 bone is semi-transparent to visualise the screw within the bone demonstrating complete concordance (sub-millimetric accuracies) of the screw with the preoperative trajectories. The 3D planning allows the depth of the screw placement to be predefined before surgery and confirmed intraoperatively with the life-size sterile model of the vertebra if required. As shown in the orthogonal planes the screw depth safely stops before the transverse foramen, therefore, preventing potential to the vertebral arteries.