Guided growth

Guiding growth by harnessing the ability of growing bone to undergo plastic deformation is one of the oldest orthopaedic principles. Correction of deformity remains a major part of the workload for paediatric orthopaedic surgeons and recently, along with developments in limb reconstruction and computer-directed frame correction, there has been renewed interest in surgical methods of physeal manipulation or ‘guided growth’. Manipulating natural bone growth to correct a deformity is appealing, as it allows gradual correction by non- or minimally invasive methods.

This paper reviews the techniques employed for guided growth in current orthopaedic practice, including the basic science and recent advances underlying mechanical physeal manipulation of both healthy and pathological physes.

Since the publication of L’Orthopaedia by Andry in 1741, correction of deformity has been linked with bone and joint surgery. Guiding growth by harnessing the ability of growing bone to undergo plastic deformation is one of the oldest orthopaedic principles. The iconic image of the crooked tree being splinted to grow straight, which represents our specialty, is the perfect representation of this principle.

Correction of deformity remains a major part of the workload of paediatric orthopaedic surgeons and recently, along with developments in limb reconstruction using distraction osteogenesis and computer-directed frame correction, there has been renewed interest in surgical methods of physeal manipulation or ‘guided growth’. Manipulating natural bone growth to correct a deformity is intuitively appealing, as it allows gradual correction by non- or minimally invasive methods.

Basic science

Heuter\(^1\) first provided a scientific explanation for the phenomenon of mechanical manipulation of bone growth in 1862, when he reported that increased pressure parallel to the axis of the epiphysis inhibits growth, while decreased pressure promotes it. Seven years later, Volkmann\(^2\) noted that changes in compressive forces cause asymmetrical growth of a joint. These observations, made almost 150 years ago, laid the foundation for the concept of physeal stapling and have influenced other aspects of paediatric orthopaedic practice.

The relationship between load and physeal modelling is more complex than the Heuter-Volkmann law would suggest. The ‘chondral modelling’ theory of Frost\(^3\) suggests that the relationship between loading and chondral growth resembles an inverted U-shape (Fig. 1). Physiological loading stimulates growth, while loads outside this range, either higher or lower, will inhibit it. Thus, minor degrees of joint incongruency, where the stresses remain within physiological limits, invoke a negative feedback in order to restore the joint to normal. Increasing incongruency results in the physis being subjected to loads outside the normal physiological range, invoking a positive feedback mechanism which results in progressive deformity.

This complex, non-linear relationship has many implications for the management of deformity, including a window outside which physeal manipulation may fail. Most importantly, it suggests that any intervention should be performed at an early stage when negative feedback correction can be harnessed. Early restoration of the mechanical axis is desirable to avoid permanent abnormality of the adjacent joint surfaces, which would otherwise lead to long-term morbidity.

Longitudinal growth is the result of the proliferation and enlargement of physeal chondrocytes, with variations in the degree of cell hypertrophy between different physes accounting for up to 50% of the difference in their growth rates.\(^4\) Cell enlargement is controlled...
by a membrane transport process, which may be hormonally regulated. The link between mechanical loading and these processes has not been elucidated fully. With such a complex interaction between mechanical forces and physeal reaction, it is not surprising that attempts to manipulate bone growth produce varied results.

Closed methods of guiding growth

The club foot or congenital talipes equinovarus (CTEV). Ponseti\(^6\),\(^7\) advanced our understanding of the anatomical abnormalities associated with the clubfoot deformity. His treatment addresses each abnormality specifically and involves serial manipulation and casting of the foot. The biological response of young connective tissue and bone to changes in the direction of mechanical stimuli results in an improvement in the deformity.\(^6\),\(^7\) MRI and CT studies have demonstrated that this treatment results in changes in shape of the individual tarsal bones, adjusting their abnormal relationships with each other.\(^6\),\(^7\) Unexpectedly, it has been noted that during treatment the affected talus grows faster than the normal contralateral side. This suggests that it is the modification of stress loads in such cases that leads to enhanced rates of growth and rapid changes in shape.\(^10\)

Developmental dysplasia of the hip (DDH). Untreated, DDH is associated with progressive anatomical abnormalities including a shallow, dysplastic acetabulum and an increase in the femoral neck-shaft angle. While the growth in height and width of the acetabulum depends on interstitial growth in the triradiate cartilage, its depth and concavity are determined by the presence of the femoral head.\(^11\) Pavlik\(^12\) realised that active movement was essential for both reduction of the hip and normal anatomical development. This formed the basis for his ‘functional method’ of treatment.\(^12\) His harness is used to guide the growth and development of the hip. Despite marked abnormality at the outset, these hips have huge growth potential and studies confirm that once reduced, they develop more rapidly than normal to attain normal indices.\(^13\)

Scoliosis. Guiding spinal growth using the technique of serial elongation-derotation-flexion plaster jackets to correct progressive infantile scoliotic deformity is well established.\(^14\) Mehta\(^15\) demonstrated successful correction in almost 70% of cases using this method and highlighted the importance of starting treatment at an early age in order to harness the maximal growth potential. A risk factor for failure, in keeping with the chondral modelling theory, was the magnitude of the deformity. The mean Cobb angle of the group in whom treatment was successful was 20° lower than that of those in which treatment failed. Others have recently confirmed these findings.\(^16\)

Bracing for adolescent idiopathic scoliosis does not influence vertebral development.\(^17\) Any correction achieved is due to positional changes of the vertebral bodies, and is therefore related to the flexibility of the curve. This may explain why a recent systematic review of the management of adolescent idiopathic scoliosis failed to demonstrate an advantage for bracing over observation alone.\(^18\)

Surgical physeal arrest (epiphysiodesis)

Permanent. The introduction of percutaneous techniques performed under fluoroscopic guidance\(^19\) has made epiphysiodesis much simpler and more reliable than the technique of epiphysiodiaphyseal fusion devised by Phemister.\(^20\) A longitudinal MRI study of knees following epiphysiodesis demonstrated that growth ceased immediately, even though evidence of early bony fusion was not seen until four months after the procedure.\(^21\) Satisfactory correction of leg-length discrepancy has been reported in 82% of cases, with asymmetrical fusion or over-correction complicating 12% of cases.\(^22\)

The main problem with epiphysiodesis is its timing. A number of methods of prediction have been developed, all based on the data of Anderson, Green and Messner.\(^23\) The accuracy of most is similar, with a significant rate of poor outcomes, with 10% to 27% > 2 cm from the predicted result.\(^24\) Using skeletal age instead of chronological age did not improve the accuracy of prediction. Nevertheless, epiphysiodesis remains the treatment of choice for a leg-length discrepancy of < 5 cm, although families must be made aware of the possibility of a poor outcome.

Temporary. Reversible, differential arrest across a physis is an intuitive, simple and appealing means to correct an angular deformity of a long bone. Implant-mediated guided growth allows this reversibility, provided neither the implant nor the associated surgery permanently violate the physis. Recent developments in implants have brought about a resurgence in interest in the concept of guided growth and expanded the indications for this form of management.

Specific implants for temporary epiphysiodesis

Staples. Haas\(^25\) first demonstrated reversible retardation of physeal growth in a series of experiments involving the passage of a wire loop around the physes of growing dogs, and then in a small clinical series. Stimulated by this work,
Blount and Clarke\textsuperscript{26} presented their early results with epiphyseal stapling in 1949 and this method of temporary or reversible epiphysiodesis remains popular. While staples have been used in the management of leg-length discrepancy, they are more valuable when used to encourage differential physeal growth for the correction of angular deformities. The technique has evolved and two extra-periosteal Vitallium staples per physis has become the standard method.\textsuperscript{27} Blount cited a personal communication with Phemister suggesting that staples should not be left in situ for longer than two years in order to ensure normal growth after removal.\textsuperscript{26} This has become the standard adopted in practice.

Experimentally, staple hemiepiphysiodesis has been shown to reduce, but not stop, physeal cellular activity.\textsuperscript{28} The staple affects the unstapled side of the physis to a lesser degree resulting in a decrease in overall bone length. Preservation of the periosteum and the perichondrial ring both on insertion and removal of the staple is important in preventing physeal fusion.\textsuperscript{29}

A long-term follow-up from Blount's unit reviewed 82 deformities of the knee in 56 patients.\textsuperscript{30} The results were deemed satisfactory in 65.9\%, improved in 20.7\% and unsatisfactory in 13.4\% with 12\% requiring revision for migration or extrusion of the staple. Rebound overgrowth after staple removal was more likely in younger children and complicated 40\% of cases. It was therefore recommended that deformities in girls < 12 years and boys < 13 years should be overcorrected. They advised against stapling in children with a skeletal age < eight years, as the results were less predictable and the consequences of premature physeal arrest more severe.

Other series have confirmed good results with staples for correction of angular deformity, with success rates of between 60\% to 80\% and low rates of extrusion or breakage of the staple.\textsuperscript{30–32} Recently, it has been reported that 50\% of cases demonstrate a clinically significant shift in the mechanical axis at the knee, particularly if the staple is used at the proximal tibia.\textsuperscript{33}

Staples are unreliable for the management of leg-length discrepancy, with rates of extrusion of up to 25\% and a third of cases requiring salvage epiphysiodesis.\textsuperscript{30}

**The 8-plate.** The staple remained the only implant designed specifically for epiphysiodesis for almost 60 years until the advent of the 8-plate (Orthofix, Verona, Italy). This is a dynamic construct consisting of a two-hole pre-contoured plate, available in two lengths (12 mm and 16 mm), with a choice of three lengths of non-locking 4.5 mm fully threaded, self-tapping cannulated screws (16 mm, 24 mm, and 32 mm) (Fig. 2). Other implants based on similar principles have recently been introduced into the market, such as the Pediplate (Orthopediatrics, Warsaw, Indiana).

The 8-plate is designed to act as a ‘tension-band’ rather than providing the compressive forces associated with a staple. Whilst a staple imposes a rigid fulcrum within the physis, the 8-plate places the centre of rotation outside it creating a longer moment arm for physeal growth, theoretically allowing a more rapid correction while maintaining overall bone length (Fig. 3).\textsuperscript{34} The ability of the screws to pivot results in lower pressure transmission across the physis, thereby reducing the risk of physeal fusion.\textsuperscript{35} Screws make the construct more resistant to extrusion than the smooth blades of a staple, particularly in younger children in whom the epiphyses are largely cartilaginous.

As one extra-periosteal plate per physis is sufficient for all but one indication (improving a flexion deformity of the knee), precise placement of the implant is straightforward even with distorted anatomy. This multifaceted improvement in versatility over staples has led to a renewed interest in guided growth, and consequently a rapid expansion of its indications.

**Indications for temporary hemiepiphysiodesis**

*The ‘sick’ or pathological physis.* Historically, hemiepiphysiodesis had been avoided in conditions associated with pathological physes, such as rickets, Blount’s disease or post-meningococcal sepsis, due to a belief that ‘sick’ physes did not tolerate direct surgical manipulation and could shut down completely. Contemporary studies suggest that this is not the case.\textsuperscript{36}

Deformities secondary to rickets can be difficult to manage. The first-line treatment must be medical replacement therapy but there is often a delay between the institution of treatment and response. During this time, a minor deformity could worsen, resulting in more complex multifocal metaphyseal and diaphyseal abnormalities which are less likely to correct spontaneously and can be difficult to correct with osteotomies. Early restoration of the mechanical axis would reduce the pathological loading and improve the chances of natural remodelling of the deformity.

Recent evidence suggests that hemiepiphysiodesis can successfully normalise the mechanical axis, resulting in an improvement of the radiological appearances of the hip and ankle physes in addition to those at the knee (Fig. 4).\textsuperscript{36} Rather than physeal shutdown, failure of the implant has been reported to be a significant problem in patients with pathological physes, with metal breakage rates of up to 44\% in Blount’s disease.\textsuperscript{29,37} Good correction was achieved
in those in whom the metalwork did not fail but predictors for failure have not been identified. In Blount’s disease, it is the metaphyseal screw that fails, and it has been suggested that this may be due to significant increases in movement of the screw as a consequence of the disorganised cellular structure and cystic degeneration often present in this condition.29 Using screws less susceptible to fatigue failure may overcome this problem.

Correction in the sagittal plane

Good results have been achieved for the correction of fixed flexion deformities of the knee using a pair of 8-plates.38 These are placed across the anterior distal femoral physis, on the non-bearing surface on either side of the patellar sulcus. In 18 patients, a mean flexion deformity of 23.4° was reduced to 8° (mean 1.4° per month). While the relative position of the patella did not change, the distal femoral physis was noted to slope downwards posteriorly but, surprisingly, posterior subluxation of the knee improved. Of these patients ten underwent concomitant soft-tissue releases and osteotomies, making it difficult to ascertain the true efficacy of the 8-plates.

Deformity in the coronal plane

Implant-mediated guided-growth has been used in a number of other situations characterised by abnormalities of the mechanical or anatomical axis, such as post-traumatic deformity, including tibia valga and cubitus varus, or longitudinal deficiency such as fibular hemimelia (Fig. 5). Although complete correction may not be achieved, in our experience the severity and complexity of a deformity is reduced, making later correction using other techniques simpler. At present, there are few reports of the results for these indications.38

The evidence for the 8-plate

There are a few reports of the outcome of temporary hemiepiphyseodesis using the 8-plate (Tables I and II).29,34-37,39 The results are promising, with all demonstrating high rates of success. However, these are small case series, only one of which is prospective, thereby providing only limited evidence to support the use of these implants. The studies are heterogenous in their reporting of pre-operative variables and outcome measures making any collective comparison between them difficult.
There is a growing consensus that the 8-plate has superseded the staple, but the only study directly comparing the outcomes of hemiepiphysiodesis with staples and 8-plates failed to demonstrate any differences between the two.\(^3\) However, the 8-plates had been used in significantly younger patients, which the authors suggest is because of ease of controlled placement.

The most significant weakness of these studies is short follow-up. Only one study focuses on the period after removal of the implant, which in our opinion is the ‘acid-test’, especially for the treatment of younger children. Only with longer-term follow-up after removal of the plate can we assess the sustained durability of correction and quantify the risks of rebound growth. This is essential information in evaluating the efficacy of 8-plate mediated deformity correction, and whether it reliably achieves the goal of avoiding osteotomy.

Ideally, a large, long-term prospective multi-centre study is required, which allows stratification of outcomes for various age groups and pathologies. This information would enable surgeons to adopt a more systematic approach to temporary hemiepiphysiodesis with these implants.

### Surgical modulation of spinal growth

Surgery for modulating spinal growth has mirrored that used for long bones with varying success. The basic premise has been that the concave side of a spinal deformity is subjected to supraphysiological compressive forces which inhibit vertebral growth. Epiphysiodesis of the convex side of a balanced, cosmetically acceptable congenital scoliotic curve (convex growth arrest) is comparatively more simple and safer than surgical reconstruction, and good outcomes have been demonstrated.\(^4\)

A variation on this theme is the suggestion that implants such as the growing rod or vertical expandable prosthetic titanium rib have some of their effect by producing distractive forces across the concave side of the curve, thereby stimulating growth. Although supported by laboratory data, this phenomenon remains to be proven clinically.\(^5\)

Since Blount’s early success with staples, surgeons have attempted similar techniques for spinal deformities but with disappointing results.\(^6\) High rates of loosening, as a consequence of the freedom of movement at each intervertebral segment, make the traditional staple unsuitable for use in the spine.

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### Table I. Summary of demographic details of studies of the 8-plate

<table>
<thead>
<tr>
<th>Author/s</th>
<th>Level of evidence</th>
<th>Number of patients</th>
<th>Age (yrs)</th>
<th>Number of deformities</th>
<th>Pre-operative deformity</th>
<th>Pathological physes (% cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stevens(^3)</td>
<td>IV</td>
<td>34</td>
<td>1.7 to 17</td>
<td>65 segments</td>
<td>7° to 30°</td>
<td>44</td>
</tr>
<tr>
<td>Burghardt et al(^2)</td>
<td>IV</td>
<td>11</td>
<td>10.2 (4.9 to 13.7)</td>
<td>17 segments</td>
<td>Mean valgus 26.3 mm; Varus 37° mm(^1)</td>
<td>0</td>
</tr>
<tr>
<td>Wiemann et al(^3)</td>
<td>III</td>
<td>n/a(^2)</td>
<td>11.1 (5.2 to 16)</td>
<td>24 knees</td>
<td>n/a</td>
<td>29</td>
</tr>
<tr>
<td>Ballal et al(^3)</td>
<td>IV</td>
<td>25</td>
<td>11.6 (5.5 to 14.9)</td>
<td>51 segments</td>
<td>Varus: 28.8° (11.1° to 53.3°); Valgus: 8.4° (3° to 25°)(^\dagger)</td>
<td>n/a</td>
</tr>
<tr>
<td>Klatt and Stevens(^3)</td>
<td>IV</td>
<td>23</td>
<td>10.8 (4 to 17)</td>
<td>40 knees</td>
<td>Flexion: 23.4° (10° to 50°)(^\ddagger)</td>
<td>4</td>
</tr>
<tr>
<td>Schroerlucke et al(^2)</td>
<td>IV</td>
<td>23</td>
<td>11 (7 to 14)</td>
<td>41 segments</td>
<td>Varus: 14.8° (22° to 10°); Valgus: 17.2° (12° to 20°)(^\ddagger)</td>
<td>58</td>
</tr>
</tbody>
</table>

* radiological tibiofemoral
\(\dagger\) mechanical axis deviation
\(\ddagger\) n/a, not available
\(\ddagger\) clinical tibiofemoral angle

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### Table II. Summary of the outcomes of studies of the 8-plate

| Author/s          | Follow-up (%) | Duration of follow-up (mths) | Successful correction (% cases) | Rate of correction (*/yr) | Complications (%)
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<tbody>
<tr>
<td>Stevens(^3)</td>
<td>100</td>
<td>14 to 26</td>
<td>97</td>
<td>n/a</td>
<td>11.7 rebound</td>
</tr>
<tr>
<td>Burghardt et al(^2)</td>
<td>79</td>
<td>9.5 (5 to 13)(^*)</td>
<td>91.00</td>
<td>n/a</td>
<td>None</td>
</tr>
<tr>
<td>Wiemann et al(^3)</td>
<td>79</td>
<td>14.1 (6 to 27)(^*)</td>
<td>8750</td>
<td>11.1</td>
<td>One screw breakage</td>
</tr>
<tr>
<td>Ballal et al(^3)</td>
<td>100</td>
<td>12.4 (6 to 32)(^\dagger)</td>
<td>n/a(^\ddagger)</td>
<td>8.4 (femur); 6 (tibia); 14.4 (both)</td>
<td>One migration; one deep infection; one rebound</td>
</tr>
<tr>
<td>Klatt and Stevens(^3)</td>
<td>78</td>
<td>13.4 (5 to 28)(^*)</td>
<td>80 (of 5 knees)</td>
<td>16.8</td>
<td>One rebound (20)</td>
</tr>
<tr>
<td>Schroerlucke et al(^2)</td>
<td>100</td>
<td>17(^*)</td>
<td>n/a</td>
<td>5</td>
<td>Implant breakage - 26 of proximal tibial plates</td>
</tr>
</tbody>
</table>

* post plate implantation
\(\dagger\) post plate removal
\(\ddagger\) n/a, information not available
The introduction of thorascopic techniques has led to a renewed interest in the use of small implants for mechanical modulation of spinal growth, and the hope of providing genuinely minimally invasive surgery. By allowing early treatment of deformity, permanent fusion and its associated complications could be avoided. The results of laboratory and clinical work have been promising.43,44

In a series of porcine experiments, custom staples secured with screws at multiple levels have been used to create spinal deformities; confirming that these implants can modulate spinal growth.43 The histology demonstrates the presence of a compressive stress-gradient, supporting the concept that scoliosis is a result of asymmetric vertebral growth which should therefore respond to differential physiological inhibition.45

In the largest clinical series, Betz et al44 reported the use of Nitinol stapling (Medtronic Sofamor Danek, Memphis, Tennessee) in 21 patients with adolescent idiopathic scoliosis. The prongs of this shape-memory alloy staple transform from straight to C-shaped at body temperature, for secure fixation in bone. Staples are passed across the physis of all vertebrae in the curve, either with thorascopic assistance or by a mini-open retroperitoneal approach to the lumbar spine. Successful stabilisation was achieved in 60% of the curves and the authors recommend this technique over bracing.

Conclusion
Guided growth is a valuable option for the treatment of many deformities in the skeletally immature patient. At present, we recommend the use of percutaneous epiphyseal stapling for correction of a leg-length discrepancy < 5 cm. For the correction of angular deformity, both staples and the 8-plate demonstrate good results, but our personal preference is the 8-plate due to its versatility. The correct timing of intervention remains the biggest surgical challenge. The basic science suggests that guided growth is most likely to be successful at an earlier stage of the deformity, but the surgeon must be aware of the risk of rebound growth. All orthopaedic surgeons who deal with children should be aware of these management options so that they may be referred to a specialist at the appropriate time, thus reducing the need for major reconstructive procedures.

A number of other experimental techniques for guided growth are in early development. These include physeal transplantation46 and biological modulation.47

The outlook for guided growth is certainly promising, but as with all new techniques, enthusiasm must be controlled whilst the results are evaluated carefully and their indications refined. Only when today’s children are adults will we know whether our actions produced the outcomes that we planned.

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