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SCIENTIFIC SECTION

Northcroft Memorial Lecture 2007. A century of progress: advances in orthodontics since the foundation of the British Society for the Study of Orthodontics

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The British Orthodontic Society invites outstanding contributors from the field of Orthodontics to give the guest lecture in memory of George Northcroft. In 2007 the guest lecturer was Professor Murray C. Meikle. The article that follows was presented as the Northcroft Memorial Lecture 2007 at the British Orthodontic Conference, Harrogate, UK, 24th September 2007.

Invited paper

Origins of the Society

On 21st October 1907, 11 dentists joined George Northcroft in his consulting rooms at 115 Harley Street, Cavendish Square, London, in response to a letter calling a meeting to discuss the formation of a society devoted to the study of orthodontics – or orthodontia as it was then called. After some discussion as to whether it was to be a specialized group, agreement was reached that it should be open to all members of the profession with an interest in the subject. Mercifully, the title favoured by Northcroft – The British Society for the Study of Odonto-prosopic Orthopaedics was not adopted, and the British Society for the Study of Orthodontia (BSSO) came into being with JH Badcock as its first President. However, Sir James Murray, foundation editor of the Oxford English Dictionary, subsequently pointed out the linguistic solecism of having a word constructed from two Greek words and a Latin suffix, and suggested that an ending in *c* would be more appropriate; the name was duly changed to the British Society for the Study of Orthodontics in 1909.

George Northcroft was born in 1869, the son of an architect and educated at The Leys School in Cambridge. While at the school he would have been taught Latin by the legendary WH Balgarnie, a schoolmaster at The Leys for 50 years and the model for Mr Chipping in *Goodbye Mr Chips* by James Hilton, a former pupil. Northcroft then took the unusual step of travelling to the United States to study dentistry at the University of Michigan in Ann Arbor, graduating DDS in 1890. He then returned to Charing Cross Hospital and the Royal Dental Hospital to continue his training, passing the LDSRCS (Eng) in 1892. Apart from a short period at Windsor, his practising life was spent in Harley Street and he remained clinically active up until his death in 1943 at the age of 74 years. In 1947 the Northcroft Memorial Lecture was established.

It was suggested that in the centennial year of the BSSO's foundation, an historical review of significant advances in the theory and practice of orthodontics would be appropriate, not an easy task given the volume of work to choose from; my selection is therefore unavoidably subjective and will disappoint many. To add some structure to a diverse body of information, the discussion has been divided into five broad categories, with inevitably some overlap.

Biological foundations

Northcroft clearly recognized the importance of understanding facial growth in his Dental Board lecture of 1924 – 'The teeth in relationship to the normal and abnormal growth of the jaws'.[1] Our knowledge of dentofacial growth and whether it can be modified, determines our clinical philosophy and treatment aims,

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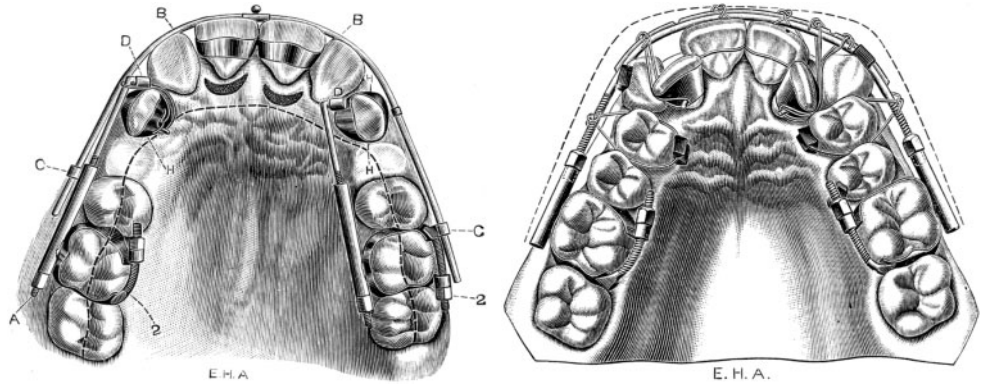


(a) (b)

Figure 1 State-of-the-art orthodontic appliances *c.* 1907. (a) Combination of traction screws and an arch bar (B) to treat a first premolar extraction case that first appeared in Angle's 6th edition of 1900; the ball at the front of the arch bar is an attachment for occipital anchorage. In Angle's 7th edition, extraction treatments were not discussed and this figure was relegated to an appendix. (b) The E-arch; expansion was provided by the ribbed arch held in position by clamp bands on the first molars. Notches were cut in the arches to prevent slippage of the ligature wires applying traction to the teeth. (Reproduced from Angle)[2]

and many of the early Northcroft Lectures were concerned with the development and growth of the jaws and dentition. It is convenient that EH Angle, the founding father of orthodontics, published his 7th Edition in 1907,[2] because it provides an ideal starting point from which to discuss the biological, and later the biomechanical aspects of orthodontics.

Angle and the 'New School'

Prior to the introduction of cephalometric radiography most orthodontic treatment was based on the non-extraction philosophy of Angle. The Angle School ridiculed claims that heredity was one of the causes of malocclusion, and considered malocclusion to be the consequence of inadequate bone growth which could be corrected by alignment of the teeth – a rather liberal interpretation of Wolff's law. If started young enough, the stimulating effects of orthodontic tooth movement and the establishment of normal occlusion would cause the jaws to grow. In other words, malocclusion could be treated without extracting teeth by growing bone.

Although all the case histories in the 7th edition involved non-extraction treatment, the appendix contains several engravings from the 6th edition, published in 1900, illustrating devices used to treat cases in which premolars had been extracted (Figure 1a). One can only speculate why Angle abandoned extraction treatment, but looking at the appliances of the day it is not hard to guess why. Closing extraction spaces must have been difficult, uprighting teeth impossible, and the results likely to have been disappointing. Angle also had a personal reason for denouncing extractions; he had extracted two upper first premolars in his wife Anna and could not keep the spaces closed.[3]

With the benefit of hindsight one should not judge them too harshly. Opposition to Darwin and Natural Selection was widespread, and Lamarckian concepts of the inheritance of acquired characteristics continued to exist well into the twentieth century. Martin Dewey, the leading Angle apologist of the time and Calvin Case's opponent at the Extraction Debate of 1911,[4] dismissed inheritance as an aetiological factor, the prevailing view being that the occurrence of malocclusion in parents and siblings was because each had experienced exactly the same environment.[5]

The introduction of cephalometric radiography

In 1937 Broadbent published his famous paper on the face of the growing child,[6] and Figure 2 played a key role in establishing the idea that the face grew downwards and forwards in an orderly, consistent manner. Although the subjects in the Bolton Study were measured longitudinally, the headfilms used to compose the figure did not come from one individual, but were representative examples of several stages; that is to say, the study was mixed–longitudinal. The figure is also androgynous; the only difference between boys and girls being one of comparative size. Given that Broadbent had developed the cephalostat to make longitudinal studies of facial growth possible, it is a mystery why he chose to present the data in this cross-sectional manner.

The first cephalometric investigation of treatment outcome in 1938 effectively destroyed the myth that orthodontic appliances could stimulate the growth of

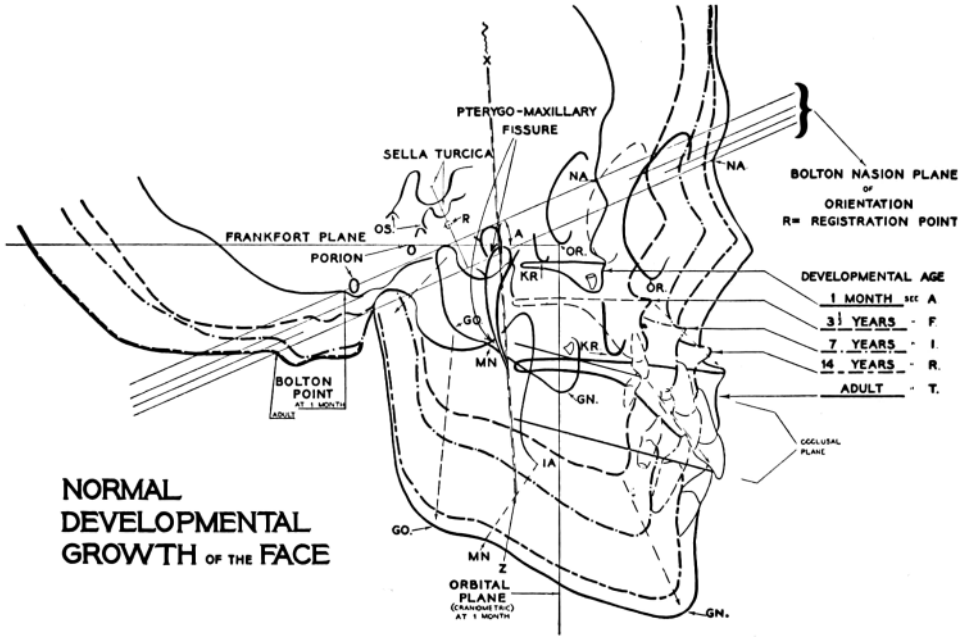


Figure 2 Growth of the face from one month to adulthood constructed from the records of subjects in the Bolton Study. This famous figure based on cross-sectional data, served to reinforce the idea that the face grew downwards and forwards in an orderly consistent manner. Subsequent studies of the facial growth pattern of individual patients showed that this concept was incorrect. (Reproduced from Broadbent,[6] by permission of the Angle Society)

bone, providing convincing proof that orthodontic treatment was limited to the dentoalveolar process and tooth movement.[7] The following year the first longitudinal study of the early growth of the head was published,[8] suggesting the growth pattern of the individual was established at an early age, and that once attained did not change. The effect of these early cephalometric studies on the orthodontic community was profound, giving rise to the linked concepts of the immutability of the facial or morphogenetic pattern of the individual, and the inability of the clinician to alter it in any way. The old dogma was consequently replaced by a new one; orthodontic treatment was restricted to tooth movement alone. Some clinicians still believe this.

Alterations in maxillary growth

It was not until the 1950s that this view began to be seriously challenged. The first convincing evidence that changes in facial growth could be achieved clinically (apart from rapid maxillary expansion) came from retrospective studies of patients that had worn headgear (HG). These demonstrated that the forward growth of the maxilla could be restrained and in some cases moved distally in relation to the anterior cranial base,[9,10] results which suggested the force had been transmitted beyond the alveolar bone to produce remodelling of the sutures attaching the maxilla to the rest of the skull.

Studies in non-human primates

These findings led to the establishment of several university-based research programmes into the effects of mechanically-induced strain on the dentofacial skeleton of *Macaca mulatta* and other monkey species. All showed that by using mechanical forces to create controlled remodelling of the facial sutures, it was possible to alter the positional relationships of the bones of the facial skeleton.[11–14] Facial sutures, being fibrous articulations, readily respond to changes in their mechanical environment.

In the 1930s Carl Breitner had provided histological evidence, first in the German literature and later in two classic papers in English,[15,16] that the effects of mechanical forces applied to the mandible were not limited to the teeth, but could alter the surface contours of the condyle and glenoid fossa (Figure 3). Every generation likes to re-invent the wheel and we were no exception. Despite advances in cephalometrics, metallic implants, vital staining and more sophisticated staining techniques, subsequent investigations added comparatively little new information to Breitner's original findings.[11,17–20] The response of the temporomandibular joint (TMJ) to externally-applied force in rat and monkey models has been reviewed recently.[21] These suggest that mandibular displacement in non-human primates initiates remodelling activity within the TMJ

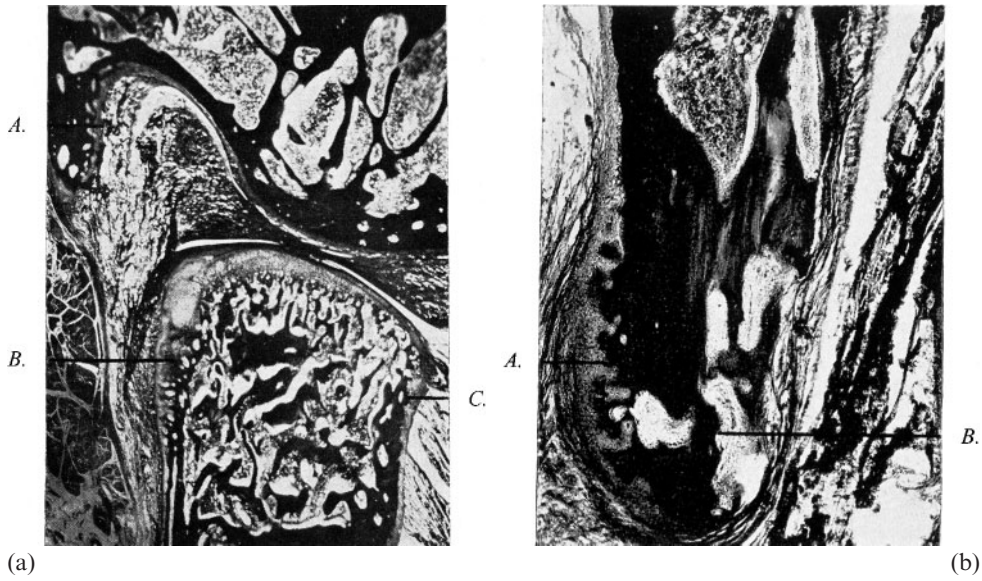


Figure 3 (a) TMJ of a young Rhesus monkey following 'jumping the bite' with cap splints for 46 days. (A – deposition of bone along the posterior wall of the glenoid fossa; B – same on posterior side of the condyle; C – resorption at the insertion of the lateral pterygoid muscle.) (b) Post-glenoid tubercle following distal displacement of the mandible. (A – deposition of bone along the posterior surface; B – resorption on the anterior surface opposite the point of maximal compressive stress.) (Reproduced from Breitner,[15] by permission of Elsevier Inc.)

and can alter condylar growth direction; this may have clinical utility in an actively growing child. However, despite claims to the contrary, there is no convincing experimental proof for condylar growth stimulation in either rodent or primate models.

The morphological approach to the study of craniofacial growth

The most important advance in cephalometry following the invention of the cephalostat was the introduction of the implant method in 1951 by Björk. Metallic implants provided stable reference points on which to superimpose maxillary and mandibular tracings, and enabled clinicians not only to distinguish between the effects of treatment and growth more accurately, but also led to a greater understanding of the growth and remodelling characteristics of the bones of the dentofacial skeleton.[22,23] It was studies such as these that identified the wide individual variation in the amount and direction of condylar growth (Figure 4), as well as the existence of maxillary and mandibular growth rotations, features of facial growth that play an important part in achieving a successful treatment outcome.

At the same time Enlow, an anatomist, was studying the patterns of surface remodelling of the bones of the face from serial histological sections of human skulls.[24] In common with all bones, enlargement of the facial

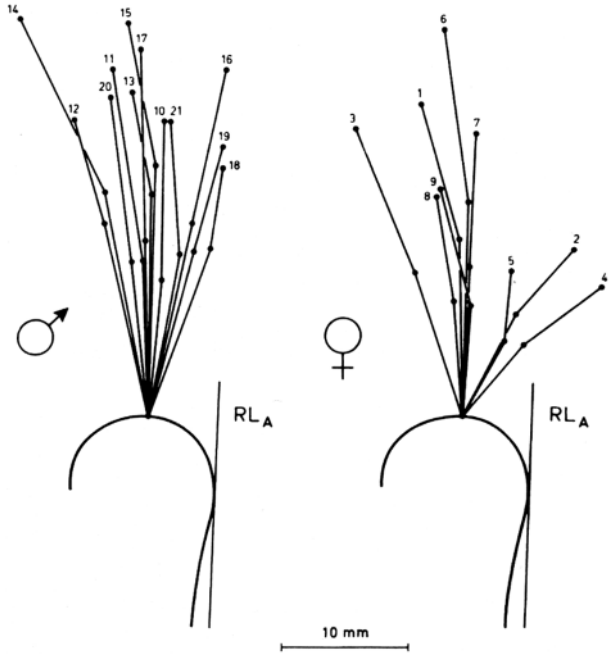


Figure 4 The wide variation in the direction and amount of condylar growth (based on mandibular tracings superimposed on implants at three-year intervals over a six-year period) is well illustrated in this sample of 12 boys and 9 girls from the Copenhagen Growth Study. (Reproduced from Björk and Skieller,[23] by permission of the American Association of Orthodontists)

skeleton does not occur through uniform periosteal deposition, but is accompanied by complex patterns of surface deposition and resorption that serve to maintain its shape and proportions as it increases in size. An observation made originally by John Hunter[25] and confirmed experimentally by Sir George Humphry.[26]

Craniofacial development and the new genetics

By the 1970s, however, it was clear that a purely morphological approach to the study of craniofacial development, form and function had reached the limit of its explanatory powers. The subject was rejuvenated by two developments. First, the demonstration that most of the bones of the head are derived from migratory neural crest cells and not from the cephalic mesoderm as previously thought. And second, advances in molecular biology enabled the principles of *Drosophila* genetics to be applied to vertebrate head development.

The vertebrate head owes its origin to the co-option of ectoderm from the neural plate to provide a second source of mesenchyme or ectomesenchyme to form cartilage, bone and dentine,[27] and is the most striking change coincident with the evolution of vertebrates more than 500 million years ago. The neural crest, the population of cells derived from the neural plate is the key to understanding the development of the head, which begins with the formation of the neural tube. Neural crest cells emigrate from the neural tube during or shortly following neural fold fusion and migrate to numerous sites throughout the body. (For a detailed discussion of the cellular and molecular basis of vertebrate head development, see Ref. 28)

The cephalic neural crest

Our current understanding of the fate of the cephalic neural crest comes largely from the work of Le Douarin and her colleagues using the quail-chick chimera model.[29,30] These have shown the extensive contribution of neural crest cells to the avian skull; in addition to the facial and visceral skeleton, the neural crest also gives rise to the bones of the membranous neurocranium (Figure 5a). Depending upon whether the bones are derived from ectomesenchyme or mesoderm, the skull can be divided into two parts: the prechordal skull anterior to the tip of the notochord (which reaches the middle of the sella turcica) and is derived from neural crest, and the chordal skull located posterior to this boundary, derived from both neural crest and cephalic and somatic mesoderm (Figure 5b). During evolution there has also been a progressive incorporation of the first five somites into the occipital region of the skull, the

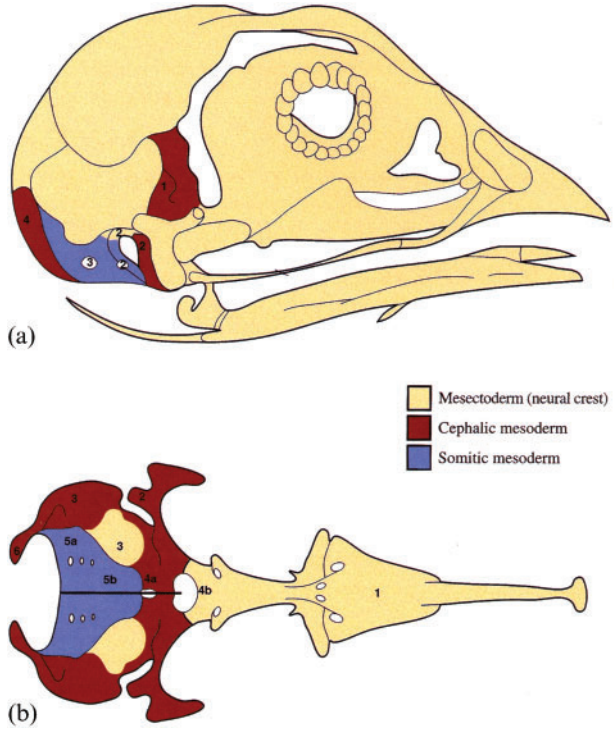


Figure 5 (a) Right external view of the skull of a bird. The bones of the lower jaw and most of the skull are derived from cells of neural crest origin. (b) Dorsal view of the chondrocranium. 1, nasal capsule; 2, orbital capsule; 3, otic capsule; 4, basisphenoid; 5, occipital; 6, supraoccipital. The black line represents the notochord, the anterior tip of which lies in the sella turcica. The prechordal skull is formed entirely by the neural crest. (Redrawn from Couly *et al.*)[30]

spheno-occipital synchondrosis representing the boundary between the cephalic and somatic mesoderm.

Hox and other homeobox genes

During development, the anteroposterior (AP) axis of the embryo of the fruitfly *Drosophila melanogaster* becomes progressively divided into a total of 14 segments by a series of segmentation genes. Segmentation genes may be sufficient to specify the body pattern of annelid worms in which most segments are alike, but in insects the segments are different and the characteristic phenotype of each segment (wings, legs, etc.) is determined by homeotic selector genes. These are clustered into two complexes, known as the homeotic complex (HOM-C), so-called because they contain a DNA sequence termed the homeobox. Remarkably, the homeotic genes that regulate the *Drosophila* body plan have been conserved during evolution and adapted to generate the complexity of form and function that characterizes mice and man. The vertebrate homologues of *Drosophila* HOM-C are

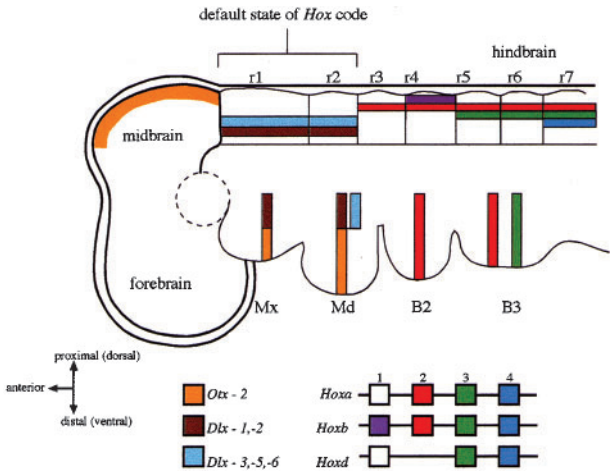


Figure 6 Schematic representation of homeobox gene expression in the branchial arches. The maxillary (Mx) and mandibular (Md) processes of the first branchial (mandibular) arch are populated by neural crest cells from the distal midbrain and rhombomeres r1 and r2. The hindbrain contributes to the proximal region (represented by the *Dlx* genes) and the midbrain crest to the distal region (*Otx*-2); in other words, crest cells populating the mandibular arch have different axial origins. Neural crest cells expressing classical *Hox* genes from r3 populate the second branchial arch and so on. (Reproduced from Meikle)[28]

known as *Hox* genes and their importance lies in the key role they play in patterning the AP axis of developing vertebrates.

In the pharyngeal arches neural crest cells are positionally specified by classical *Hox* genes expressed in nested domains in hindbrain segments known as rhombomeres (r) (Figure 6). Populations of neurogenic and mesenchynal crest cells carry this branchial *Hox* code as they migrate to the periphery, which accounts for the co-ordination of rhombomeric and pharyngeal segmentation.[31] However, as Figure 6 shows, *Hox* genes are not expressed by neural crest cells migrating from r1 and r2 into the first branchial arch. The maxillary and mandibular processes are populated by crest cells from the midbrain and r1 and r2 expressing homeobox-containing genes that are not related to *Drosophila* HOM-C; these include members of the *Otx, Dlx* and *Msx* families.[32–34]

Msx and *Dlx* genes are involved in patterning of the first branchial arch (Figure 7), and play key roles in epithelial-mesenchymal interactions. The lower panel shows the domains of expression in the mandibular processes, part of what Paul Sharpe has referred to as the odontogenic homeobox code[35] and the reason why we have incisors at the front and molars at the back of

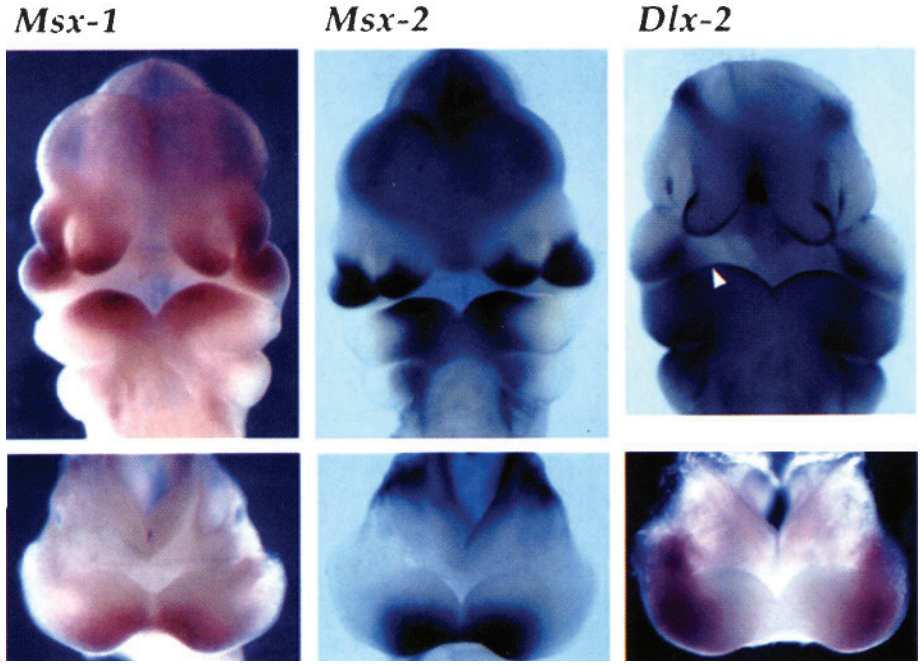


Figure 7 Expression patterns of *Msx*-1 and *Msx*-2 in the distal (ventral) regions, and *Dlx*-2 in the proximal (dorsal) regions of the ectomesenchyme of the maxillary and mandibular processes; 10.5-day mouse embryo. Top, viewed from the ventral aspect; bottom, the mandible removed and viewed from the oral aspect. Whole mount *in situ* hybridization using digoxygenin-labelled RNA probes. (Courtesy of Bethan Thomas and Paul Sharpe, King's College London Dental Institute)

the mouth. Mutations in the human *Msx*-1 gene have been shown to cause lateral incisor and second premolar tooth agenesis, and to be strongly linked to clefts of the primary palate.

Malocclusion as a biomechanical problem

The evolution of fixed appliances

The state-of-the-art non-extraction appliance in 1907 was the expansion or E-arch of Angle (Figure 1b). Angle's next major development was the Pin-and-Tube designed for moving roots as well as crowns. The appliance however, was difficult to use (the pins had to be removed and resoldered) and was replaced in 1915 by the Ribbon Arch bracket that enabled the teeth to slide along the wire.[36] In 1928 Angle introduced the Edgewise Arch Mechanism, 'the latest and best' which was a considerable advance because it enabled force to be applied in all three planes of space.[37] It is somewhat ironic that by inventing the Edgewise appliance with three-dimensional control of tooth movement, Angle unwittingly provided the means to treat extraction cases efficiently and to a high standard. And the person to do this was Charles Tweed, one of Angle's last students, who had worked closely with him to field test the appliance.

The question of extractions

Tweed followed the Angle philosophy diligently for several years and then recalled 70% of his patients; he found that of those who had been out of retention for 2–5 years, his success rate was less than 20%. After analysing the cases, Tweed found a correlation between facial balance and the position of the mandibular incisors with respect to basal bone, and to achieve this had begun to extract first premolars.[38] This did not go down well with his colleagues in the Angle Society, which by this time had begun to acquire some of the hallmarks of a cult. Tweed's iconoclastic extraction philosophy coupled with his demonstrable clinical ability eventually made an impact, however, gaining many supporters, to such an extent that in 1944 the debate known as the 'Extraction Panel' was held in Chicago at the annual meeting of the American Association of Orthodontists.[39]

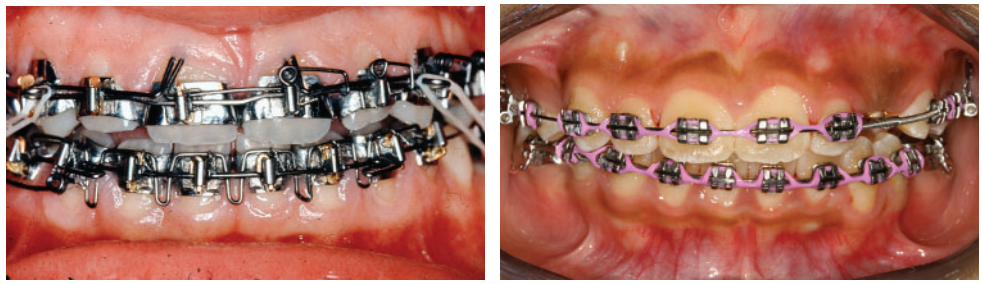
Another student of Angle who abandoned non-extraction treatment was Raymond Begg. Begg had made an extensive study of Australian aboriginal skulls including tooth wear; the food of Stone Age man was hard, coarse, fibrous and gritty leading to marked occlusal and interproximal wear. Begg argued that because Stone Age Man's dentition was reduced by interproximal wear, orthodontists had a well-founded scientific precedent for extracting teeth.[40]

The problem with the non-extraction/extraction controversy was that the arguments were largely personality driven and anecdotal, and to some extent still are. Both sides lacked the objective documentation of post-retention results necessary to prove their case. What was the evidence base for their respective points of view? The aim of premolar extractions was to effectively treat patients with arch length discrepancies and bimaxillary protrusion, the rationale being to ensure post-treatment stability and improve facial aesthetics. However, while Tweed, Begg and others were key figures in establishing extraction therapy as a respectable clinical practice during the 1950s, they failed to address the next logical question:[41] were premolar extraction cases more stable after retention, or were they also liable to relapse? As it turned out, the assumption that the extraction of premolars resulted in a more stable occlusion, particularly of the lower incisors, proved to be unfounded.[41,42]

The tyranny of fixed appliances

The recommended patient load for an orthodontist in the 1960s was 100 fixed appliance cases, and unless one practised orthodontics in those days, it is difficult to appreciate how labour-intensive and time-consuming archwire changes could be (Figure 8). However, in the 1970s orthodontics was liberated by the following events: (1) the introduction of the acid-etch technique for bonding brackets directly to enamel; (2) the development of the Straight-Wire or pre-adjusted appliance; and (3) the availability of preformed, highly flexible, nickel–titanium (nitinol) archwires.

Arguably the most important of these was the introduction of the Straight-Wire Appliance in 1970. It evolved from Andrews 'six keys to normal occlusion', the aim of the appliance being to consistently produce an ideal occlusion in which all six occlusal features would be present.[43,44] Standard edgewise archwires with anterior torque required fifteen or more bends in the upper arch and eight or more in the lower, and for the Tweed technique with tip-back bends the figure reached over 20. By incorporating in–out, tip and torque into the bracket design, wire bending was minimized and sliding mechanics could be used routinely to close extraction spaces, virtually eliminating the need for closing loops and up-righting springs. Although some may regret the decline in manual dexterity required for contemporary practice, orthodontic treatment has been transformed for both clinician and patient; chairside time has been



(a) (b)

Figure 8 (a) Fixed appliance (Begg) *c.* 1970. The use of torquing auxiliaries, up-righting springs and multi-looped archwires made adjustments to the Begg appliance frequently more laborious than standard edgewise. (b) Contemporary fixed appliance. By the end of the decade, orthodontic practice had been transformed by the acid-etch technique for direct bonding, plus the introduction of the pre-adjusted appliance and preformed nitinol archwires (Courtesy of Dr Low Hwee Hiang)

reduced, patient load increased, and treatment outcome is more predictable, developments that are likely to accelerate with the introduction of orthodontic auxiliaries.

Dentofacial orthopaedics

At the same time that fixed appliance systems were being developed in the United States, a parallel philosophy of treatment – dentofacial orthopaedics was evolving in Europe. This method was based on removable functional appliances, intended as the name implies to move bones as well as teeth. The earliest functional appliance, the Monobloc, was introduced by the French stomatologist Pierre Robin in the early 1900s, and was designed to correct the jaw relationship in patients with the syndrome he had described in infants with mandibular retrognathia and glossoptosis (clefting of the secondary palate was added in the 1960s). However, the first functional appliance to gain widespread clinical use was the Activator, designed by Viggo Andresen and developed in collaboration with Häupl into the Norwegian system of functional jaw orthopaedics.[45]

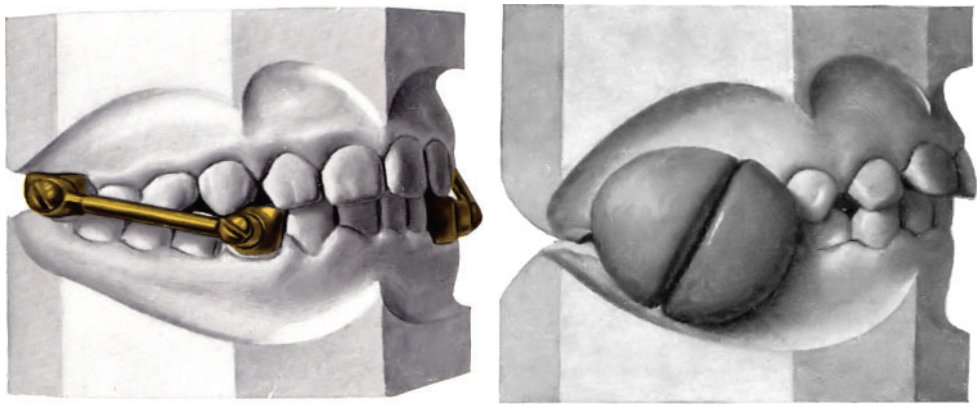
After World War II and with Europe in ruins, functional appliances provided the means to treat large numbers of patients in socialized healthcare systems, in countries with limited financial resources and manpower. During this post-war period, functional appliances underwent numerous eponymous modifications, particularly in Germany by Häupl, Bimler, Balters, Fränkel and others.[46] The proposal that class II malocclusions were corrected by stimulating condylar growth seems to have arisen at this time and became an article of faith for many.

For most of the twentieth century, however, with a few exceptions, functional jaw orthopaedics was studiously ignored by the mainstream orthodontic community in North America, being seen as the preserve of eccentric *émigrés*, paediatric dentists and others lacking recognized specialist orthodontic training. Nevertheless, whatever the more fanciful claims made on their behalf, it was clear that functional appliances could produce dramatic changes in jaw relationship in many patients not possible with fixed appliances, a technology that had largely stopped evolving. In the 1980s there was a synthesis of North American fixed appliance systems with European functional appliances, and the term growth modification replaced growth stimulation to describe the objectives of dentofacial orthopaedics. Rationalism it seemed had finally prevailed.

The Andresen Monobloc and its variants such as the Bionator and Harvold Activator are essentially passive in action. Increasingly popular are more active appliances such as the Herbst and twin-block, based on the principle of 'jumping the bite' originally proposed by Norman Kingsley. Although Emil Herbst had introduced his fixed-functional system in the early 1900s,[47] little was known about the appliance until it was rescued from obscurity by Pancherz.[48] The twin-block technique developed by Clark,[49] uses inclined occlusal planes to displace the mandible forwards, a principle similar to the appliance illustrated in Herbst's textbook of 1910 (Figure 9).

Mini-implants for orthodontic anchorage

The most important development in clinical practice over the past decade has been the use of titanium mini-/micro-screws as temporary anchorage devices.[50] Mini-implants have developed from maxillofacial fixation techniques and considering how long implants have been used in restorative dentistry, their introduction into orthodontics seems to have been remarkably slow; perhaps we were distracted by a preoccupation with osseointegration. Their advantage is that they are small (typically 1–2 mm in diameter, 8–15 mm in length) and



(a) (b)

Figure 9 Appliances designed to treat class II malocclusions. (a) The original Herbst appliance consisted of a telescopic hinge attached to bands on the maxillary first molars and mandibular canines. (b) Inclined planes made of India rubber attached to bands cemented to maxillary and mandibular posterior teeth, were also used to displace the mandible forwards. (Reproduced from Herbst)[47]

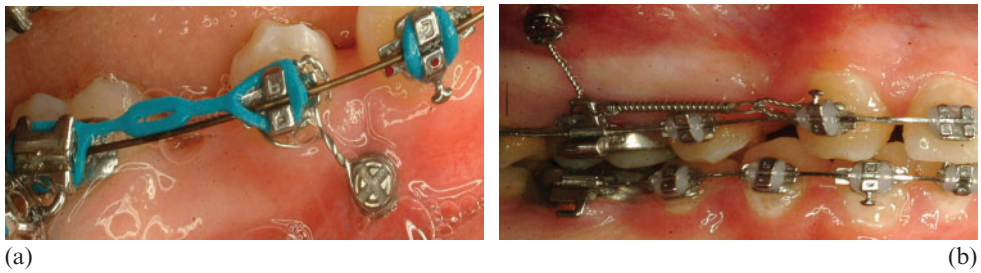
relatively simple to insert and remove under local anaesthesia. As they depend on mechanical retention, mini-implants can be loaded immediately after insertion if required and provide osseous anchorage that is not dependent on patient compliance (Figure 10). Regrettably, some orthodontists have forgotten they are also dental surgeons and refer patients to have implants inserted by periodontists and oral surgeons.

The Interventional Procedures Advisory Committee (IPAC) of the National Institute for Health and Clinical Excellence (NICE) has recently reviewed the procedure including the relevant literature and issued a consultation document about its safety and efficacy. IPAC will consider the consultation comments and produce a Final Interventional Procedures Document to be considered by NICE before issuing guidance regarding their use in the National Health Service (NHS).[51] At the time of writing they had not yet reported.

The biology of tooth movement

The first experimental study of tooth movement, '*Einege Beiträge zur Theorie der Zahnregulierung*' (Some contributions to the theory of tooth movement) was published in three-parts by Carl Sandstedt in 1904–1905.[52] After more than 100 years the literature is understandably extensive and has recently been reviewed at length by the present author.[53] We now have a reasonably good understanding of the sequence of events involved at the tissue and cellular level, and in common with the rest of the biological sciences the methodology of tooth movement research has become progressively more reductionist. The techniques of reverse-transcription polymerase chain reaction (RT-PCR) and *in situ* hybridization to detect mRNAs of interest has revolutionized tooth movement studies, and an expanding list of antibodies and enzyme-linked immunosorbent assays (ELISAs) directed against human and animal proteins have facilitated their identification in tissue sections and culture supernatants.

One of the advantages of the commercialization of molecular biology is that clinical academic departments can now study genomics and proteomics without having a large well-founded laboratory and with limited financial resources and technical help. Figure 11 is from recent work carried out by orthodontic DClinDent



(a) (b)

Figure 10 Mini-/micro-screws that depend on mechanical retention are particularly useful for providing anchorage in hypodontia patients where it is desirable to close spaces from behind in: (a) critical anchorage cases, or (b) to intrude teeth (Courtesy of Drs Ross Anning and David Wescott)

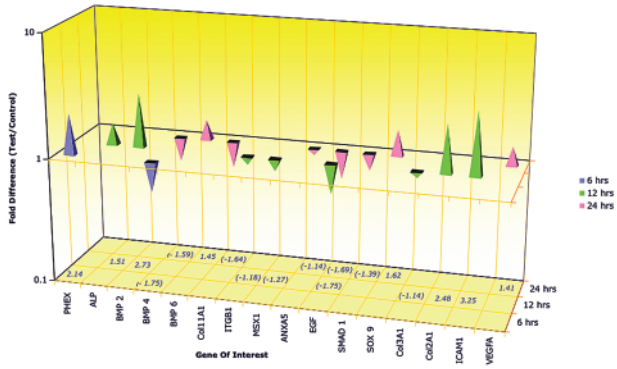


Figure 11 Mechanoresponsive osteogenic genes. Three-dimensional profiles of genes showing a statistically significant ($P<0.05$) up- or down-regulation of mRNA expression of 16 genes in response to a uniaxial, cyclic tensile strain of 12% applied to human PDL cells *in vitro*. Two cell adhesion molecules, three *BMP*s, *MSX1* and *SOX9* were among the genes whose regulation appears to be sensitive to changes in their mechanical environment. Fold-differences are represented on a logarithmic scale; values on the graph floor in parentheses are displayed for negatively regulated genes. (Reproduced from Wescott *et al.*)[54]

students at the University of Otago,[54,55] in which human periodental ligament (PDL) cells were subject to cyclic tensile strain and the RNA extracted. The samples were then screened by Superarray Bioscience Corporation (Fredrick, MD, USA) for the expression of 78 genes of osteogenic significance using real time RT-PCR, technology that enables interacting cytokine networks to be studied instead of just individual mediators. Although significant progress is being made in understanding how cells respond to mechanically induced strain at the molecular level, our understanding of what is, after all, a very complex biological process remains far from complete. This is true of the remodelling dynamics of both the PDL and alveolar bone.

Multidisciplinary treatment

In the English-speaking world, multidisciplinary treatment involving the head and neck began during World War I with the remarkable collaboration of Sir Harold Gillies and Sir William Kelsey Fry. Many of the techniques developed at the Cambridge Hospital, Aldershot and later at the Queen's Hospital, Sidcup by the British, Canadian, Australian, New Zealand, and later the American face and jaw teams treating soldiers with facial trauma, provided the basis for later civilian practice.[56]

Cleft lip and palate

Cleft lip and palate care is the ultimate multidisciplinary treatment, and orthodontics plays the key role in patient management and clinical audit from birth to adulthood. The most important development in the delivery of cleft lip and palate treatment in the United Kingdom has been the recent rationalization of the service within the NHS. Following an evaluation of the outcomes of cleft care in the UK compared to other European countries, the Clinical Standards Advisory Group (CSAG) report on cleft lip and palate services (1998) recommended concentrating surgical treatment to between 8 and 15 designated centres nationally, staffed by two cleft surgeons per unit dealing with 80–100 new cases each year.[57–60] This was based on evidence that better clinical outcomes were obtained in larger centres where surgeons operate on a sufficiently large number of patients each year to maintain their expertise. Public consultation, hospital bureaucracy, inter-professional rivalry and self-interest have delayed the implementation of such a radical restructuring proposal and there is a perception that the goals of CSAG have yet to be met. This is not surprising given the complexity and long-term nature of cleft management, and the difficulty of integrating plastic and maxillofacial surgery, orthodontics, paediatric dentistry, ENT/audiology and speech therapy.

Orthognathic surgery

Thirty years ago the involvement of orthodontics in orthognathic surgery was not routine. The change came with an increasing number of orthodontists trained in fixed appliances, thereby enabling skeletal discrepancies to be accurately corrected in all three dimensions. A variety of surgical operations mainly involving the mandible had been devised by Vilray Blair and Kazanjian in the United States, and Wassmund, Schuchardt and others in Europe during the first half of the twentieth century. Nevertheless, it was the introduction of the bilateral sagittal split osteotomy by Trauner and Obwegeser,[61,62] and later the Le Fort I osteotomy,[63] together with the surgical techniques developed by Tessier for the treatment of craniofacial anomalies,[64] that enabled orthognathic surgery to evolve into the reliable, double-jaw procedure it has become today. The most recent innovation has been the introduction of distraction osteogenesis for the correction of skeletal deformities, a development of the Ilizarov technique for lengthening long bones.

Epidemiology and orthodontics

In *The Rise and Fall of Modern Medicine*, James Le Fanu, who writes a weekly medical column in *The Daily Telegraph*, has argued that with the decline in

therapeutic innovation in medicine since the 1980s, two specialties that up until that time had played a very marginal role in post-war medicine, epidemiology and genetics, have filled the vacuum.[65] Whether or not one agrees with Le Fanu's basic thesis, it is true that epidemiology (the study of factors affecting the health and illness of populations) has had a considerable impact on orthodontic practice and health management over the past 20 years. The literature is increasingly concerned with evidence-based treatment, as well as psychosocial questions such as facial attractiveness, psychometric assessments for orthodontic and orthognathic patients, and the impact of malocclusion and its treatment on quality of life. The discussion here will be limited to orthodontic indices and randomized clinical trials.

Orthodontic indices

Orthodontic indices are not new. Early attempts included Grainger's Treatment Priority Index (1967), Salzmann's Handicapping Malocclusion Assessment Record (1968) and Summer's Occlusal Index (1971). The aim of orthodontic indices is to: (1) identify those patients likely to benefit most from orthodontic treatment, and (2) provide a numerical score to assess the degree of improvement, and therefore the quality and effectiveness of treatment. These are matters of considerable interest to providers of third-party payment schemes such as governments and insurance companies.

The three most widely used indices in both the UK and abroad are currently the Index of Orthodontic Treatment Need (IOTN),[66] the Peer Assessment Rating (PAR),[67] and most recently the Index of Complexity, Outcome and Need (ICON).[68] From 1st April 2006 the use of the IOTN was compulsory for all NHS-funded orthodontics in the UK, and is increasingly used in university- and hospital-based training programmes to triage patients. However, these are quantitative measures developed by clinicians, whose views of a successful outcome may not coincide with those of the patient. Increasingly, a patient-based qualitative approach to assessing the process and outcome of orthodontic treatment is evolving, based on questionnaires, structured interviews and quality of life indicators,[69–71] and is a trend that is certain to continue.

Randomized clinical trials

The first randomized clinical trial (RCT) was carried by Sir Austin Bradford Hill in 1946 when he was asked by the Medical Research Council to test the effectiveness of streptomycin in the treatment of pulmonary tuberculosis. Apart from the fact Hill wanted to use randomization as a method, there was insufficient streptomycin available at the end of the War to give it to all the patients that needed it, thereby making a virtue out of a necessity. Hill was Professor of Medical Statistics at the London School of Hygiene and Tropical Medicine, a statistician who avoided almost all mathematical formulae and cautioned against confusing statistical precision with validity. This is worth remembering when next reading an article claiming to show statistically significant differences in some parameter at the 0.001 level or greater, based on anatomical landmarks with measurement errors exceeding 1.0 mm. He also listed nine criteria for assessing evidence of causation, several of which are relevant to orthodontic RCTs.[72]

Nowadays the RCT is seen to be the 'gold standard' for analysing treatment outcome and for many the only valid source of clinical data. The scientific worth of the retrospective study, the traditional method used to evaluate orthodontic treatment outcome has been criticized for a number of reasons (selection bias, inadequate sample size, lack of contemporaneous controls, poor experimental design) and fallen out of favour. These are perfectly valid criticisms, but do not confer on us the freedom to ignore the knowledge we already have. In the Brave New World of evidence-based practice, one is bound to ask – how good is the evidence?

Randomized clinical trials in orthodontics

Randomized clinical trials of orthodontic treatment have been limited in number and most have been concerned with evaluating the effect of various appliances on dentofacial growth, particularly that of the mandible (Table 1). The first was undertaken in 1967 by Jakobsson,[73] a man clearly ahead of his time. Sixty subjects aged 8–9 years with a class II division 1 malocclusion, were randomly assigned from triads of children to an Andresen Activator, HG, or control group. Both HG and activator treatments were found to have a distalizing effect on the maxilla, but the study did not support the hypothesis that Activator treatment altered condylar growth. A similar methodology was used by Nelson *et al.*[74] in 42 children aged 10–13 years, the subjects in each triad being assigned to a Frankel FR-2, Harvold Activator or control group. Neither appliance was found to alter mandibular growth.

The most widely publicized RCTs have been the North Carolina and Florida studies, testing the effectiveness of HG and the Bionator in stage 1 of a two-stage treatment protocol for class II division 1

malocclusions,[75,76] and the multi-centre twin-block trial carried out in the UK.[77] The general conclusion seems to be that a two-stage treatment started in the mixed dentition is no more clinically effective than one-stage treatment started in the early permanent dentition, and has been interpreted by some to indicate that functional appliances have no place in the management of class II malocclusions. A recent Cochrane review of two-stage treatment has also shown there are no advantages in providing orthodontic treatment in two stages over providing treatment in one stage when the children are in early adolescence.[78]

One gets the impression that RCTs which originally set out to test the ability of various orthodontic appliances to modify dentofacial growth, seem to have turned into a debate about the merits of two-stage treatment in the management of class II malocclusions; these are two separate issues. Optimal conditions for achieving growth modification occur when treatment coincides with the pubertal growth spurt and ideally peak height velocity (PHV); it is clear from Table 1 that the ages of many of the participants in orthodontic RCTs were some distance from achieving PHV. Also muddying the water is the fact that two-stage treatment means different things to different people. If two-stage means starting appliance therapy at the age of 7–9, followed by a break of 2–3 years before starting a second stage with fixed appliances, this is clearly an inefficient and costly way to deliver a service. On the other hand, to many clinicians including the present author, two-stage means a class II treatment protocol involving a preliminary phase of functional appliance treatment in the late mixed dentition, followed in tandem by fixed appliances and a total active treatment time of 24 months. Like many things in life, it's a question of timing.

We treat individuals, not averages

The orthodontic RCTs undertaken to date suffer from two major structural defects: the cross-sectional nature of the data, and the tendency to focus on mean or average changes. The mean is a statistical artefact designed to produce order from large amounts of population data such as height; given the small sample sizes typical of orthodontic RCTs, very few patients are likely to show the mean change. To quote JRE Mills: 'The mean is a lonely place to be'. It was recognized as long ago as 1892,[79] that treating growth values cross-sectionally and simply taking the average, flattens out individual variation, and the reason why Boas insisted that longitudinal growth studies were needed to understand the dynamics of growth. The subject is discussed at some length by Tanner, particularly in relation to growth velocity curves.[80] Clinicians treat individuals and individuals need to be studied longitudinally.

If one adds to the above: (1) variability in the timing, magnitude, direction and duration of pubertal dentofacial growth, (2) a mixed study sample of male and female patients, characterized by sexual dimorphism in the onset of their pubertal growth spurt of up to two years, (3) the inherent inaccuracy of the cephalometric method (the measurement errors may exceed the growth changes one is hoping to identify), (4) the failure to measure cephalometric radiographs 'blind', thereby eliminating subjective bias, and (5) the questionable validity of the measurements themselves used to quantitate change, particularly of the mandible,[81] it is hardly surprising that the conclusions of RCTs have not been as clear-cut as might have been expected. Unlike a laboratory experiment in which it is possible to limit the difference between experimental and control groups to the single factor being investigated, in a clinical trial an

Table 1 Randomized clinical trials of class II treatment: effect on mandibular growth. Reproduced from Meikle.[21]

Study and analysis	Appliance	Number treated/control	Age	Change* (mm)
Jakobsson (1967)[73] Change in Pog	Andresen activator	17/19	8.5 (mean)	NS
Nelson *et al.* (1993)[74]	Fränkel FFR	13/17	11.6 (mean)	NS
Co–Pog	Harvold activator	12/17		
Tulloch *et al.* (1997)[75] Co–Pog	Bionator	53/61	1 year pre-PHV	1.33†
Keeling *et al.* (1998)[76] Johnston analysis	Bionator	78/78	9.6 ± 0.8	0.8†
Pancherz (1982) Pancherz analysis	Herbst	22/20	12.1 ± 0.11	2.2
Lund and Sandler (1998) Ar–Pog	Twinblock	36/27	12.4 (mean)	2.4
O'Brien *et al.* (2003)[77] Pancherz analysis	Twin block	73/74	8–10 (range) 9.7 (mean)	1.55

*Mean differences between experimental and control groups.
†Mean annualized change (mm/year). In the Pancherz (1982) study, the treatment time was 6 months.
NS: not significant; all other differences are small but statistically significant. PHV: peak height velocity.

orthodontic appliance is just one of several variables affecting the outcome.[82] *Homo sapiens* is characterized by endless anatomical and physiological variation, and the greater the variation between individuals, the harder it is to demonstrate that a difference in treatment effect is significant or does in fact exist. The key to understanding how patients respond to treatment in all branches of medicine is variation, variation, variation. Trying to establish the extent to which functional appliances can alter dentofacial growth is an exceedingly complex issue, many aspects of which have simply been ignored – and is the reason why many clinicians have difficulty reconciling the findings of orthodontic RCTs with their own clinical experience.

Conclusions

There seems little doubt that George Northcroft and the other founder members of the BSSO would be impressed by the progress made in orthodontic practice since 1907, particularly in the treatment standards that are now routine and with the integration of orthodontics into the management of complex malocclusions and craniofacial anomalies. Many significant developments, predominantly in technology were made during their lifetime, but the pace of advancement accelerated following World War II with the expansion of university-based training programmes linked to the growth of basic and applied research.

However, they might be surprised by developments paralleling medical practice in which many chairside procedures have been delegated to auxiliary personnel. With the introduction of orthodontic auxiliaries and combined bachelor of oral health (BOH) degrees in dental therapy and dental hygiene in several countries, this is a trend that will increase. What impact a three-year BOH will have on the five-year Bachelor of Dental Surgery (BDS) degree, manpower planning and future dental practice remains unclear, but it is doubtful the economic message as far as training numbers and the cost of health delivery will be lost on governments. It is also likely to impact on specialist training, at least that element funded from the public purse. Nevertheless, all this remains idle speculation. The best advice was offered by Sam Goldwyn many years ago: 'never make predictions – especially about the future'.

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