The word scoliosis is derived from the Greek word σκολίωσις, skoliosis, meaning bent or crooked. Multiple pathologies can cause a scoliotic deformity. Neuromuscular scoliosis is caused by disorders such as Duchenne muscular dystrophy, congenital scoliosis by different congenital abnormalities (e.g. hemivertebrae), and syndromic scoliosis by a variety of connective tissue diseases such as Marfan. This thesis will focus on the most common type of scoliosis: adolescent idiopathic scoliosis (AIS), which has no known cause, and more specifically on the surgical treatment of this deformity. This chapter provides an introduction to the natural history, epidemiology, radiological evaluation, and treatment options.

AIS is characterised by a deformity of the spine and trunk (Figure 1). The Scoliosis Research Society defines scoliosis as a curvature of the spine of >10° Cobb angle (Figure 2) [1]. AIS is a diagnosis of exclusion, i.e. other potential causes (e.g. congenital or neuromuscular) must be ruled out. The term ‘idiopathic’ describes the unknown aetiology and ‘adolescent’ refers to the patient group aged 10 to 17 years old [1]. Despite years of research on potential factors that cause scoliosis, no evidence for a single causal factor has been found. At present it is thought that AIS has a multifactorial aetiology in which metabolic, neuromuscular and genetic factors, and more recently, the unique alignment of the human spine are thought to play a role [2–4].
Natural history
The most common initial presentation of an AIS patient in an (orthopaedic) outpatient clinic is a female with an asymmetrical trunk and a right-sided thoracic scoliotic curve. The adolescent patients complain of a disfiguring shape of their back, ribs, and waist and an uneven shoulder level (Figure 1). Besides ill-fitting clothing, this results in an impairment of self-image and some patients suffer from back pain [6,7].

If left untreated into adulthood, AIS patients report decreased levels of self-image, perceive themselves as relatively unhealthy, have increased levels of back pain, and feel limited in their level of physical activity [8–11]. Female AIS patients report slightly higher rates of nulliparity and infertility treatment compared to healthy controls [10,12]. Most patients are employed and married [10,12]. Also, the majority of patients have mortality rates similar to the unaffected population whereas patients with severe thoracic deformity >80° are at risk of developing severe cardiopulmonary pathologies [10,13–15].

Epidemiology
Approximately 0.5–7.5% of adolescents suffer from AIS (cut-off ≥10°), with its prevalence varying substantially between geographical locations around the world [16–18]. The prevalence of curves >20° is 0.2–0.5%, whereas for more severe curves of >40° the prevalence decreases to 0.04–0.3% [16]. AIS disproportionally affects females. In patients with curves 11–20° the female: male ratio is 1.4:1, while in curves >40° this substantially increases to 7.2:1 [16].

The risk of curve progression after initial diagnosis is mainly dependent on age and curve severity [19,20]. Of all patients with curves between 20–30° at the onset of puberty approximately 75% will progress to a threshold requiring surgical intervention. This risk increases to 100% if the curve measures >30° at the onset of puberty. At final skeletal maturity most curves <30° remain stable, while curves >50° progress at 0.75–1° per year during adulthood [21].

Radiological evaluation
Standard radiological evaluation consists of a posteroanterior radiograph of the spine. The angle between a line drawn parallel to the superior endplate of the upper most tilted vertebral body and a line drawn parallel to the inferior endplate of the most tilted lower vertebral body is referred to as the Cobb angle (Figure 2). AIS is not only characterized by a lateral deviation in the coronal plane, but also a rotation of the vertebra in the transversal plane (the horizontal plane) and a flattened sagittal profile (a vertical plane that divides the body into a left and right halve). Although cheap and easily available, 2D radiographs fail to capture the true 3D nature of the deformity [22,23].

Computed Tomography imaging produces images in three dimensions and can thus better appreciate the vertebral rotation and sagittal deformity, but for routine application the radiation exposure is too high. Novel imaging systems like bi-planar low-dose radiographs can also produce reconstructed 3D images from 2D images with far less radiation exposure and its application in scoliosis evaluation and treatment is expanding [24–26]. With a similar goal, the use of ultrasound is under investigation, but its use in daily clinical practice is currently limited [27,28]. If a scoliosis has been identified and ‘red flags’ such as back pain, signs of neurological abnormalities, or abnormal curve types are present then Magnetic Resonance Imaging can be used to identify an underlying disease [29,30].

Radiological classification
The Lenke classification system is frequently used to determine the curve type [31]. It aids in standardized communication and clinical decision-making, because different curve types require different treatment strategies. The system is based on the spinal deformity in the frontal plane, the alignment in the sagittal plane, and the flexibility of the curve on bending radiographs. It describes the spinal deformity of a patient by identifying two curve types; (1) the major curve: the curve with the largest Cobb angle, always considered structural, and (2) the minor curve: a smaller curve, either structural or non-structural. A non-structural curve is defined as a curve that reduces to <25° on radiographs with the patient bending to the convex side. The six Lenke subtypes each represent a combination of structural and non-structural curves, and curve locations (i.e. thoracic or thoracolumbar/ lumbar). The Lenke classification system is limited to a 2D evaluation of the deformity. Improvements in imaging techniques have the potential to appreciate better the 3D characteristics of the deformity and hopefully provide improved options for diagnosis, prediction of curve progression and treatment [32].
Non-operative treatment
Non-operative treatment is mainly based on brace therapy. The goal is to prevent curve progression and the need for surgery. The treatment is tailored to the location of the curvature, curve severity, and risk of curve progression. Furthermore it depends on patient compliance and, most importantly, patient preference. For skeletally immature patients with a Cobb angle <25° watchful waiting with regular follow-ups every 6-12 months is sufficient [33,34]. Patients with curves between 25-45°, aged 10-15 years and who are skeletally immature can be treated with a brace [33–36]. Achieving compliance with brace therapy is challenging due to the psychological stress and physical discomfort, while treatment success is highly dependent on the number of hours the brace is worn [37–39].

Operative treatment - technique
Surgical treatment may be considered for patients with curves exceeding 45-50° at skeletal maturity, because of a high risk of curve progression [21,33,34]. Surgery is performed to (1) prevent curve progression, (2) correct the deformity and improve spinal alignment, (3) improve cosmetic appearance and psychosocial functioning, and (4) prevent pain or cardiopulmonary dysfunction later in life [40].

The first report of surgical fusion (arthrodesis) of spinal deformities dates back to as early as 1911, but this technique only aimed at preventing curve progression and was hampered by a lack of correction and high complication rates [41]. Fifty years later Harrington developed distraction rods, attached to the spine with hooks, for the first time allowing for correction of the lateral curvature [42]. Although this was a major improvement the limited fixation, lack of true 3D correction, decrease in sagittal profile (flat back syndrome), and the risks of increased vertebral rotation and rib deformity formed significant limitations to this technique [43,44].

The current most commonly used techniques aim at achieving a correction of the deformity in all three planes, creating a balanced spine, and maintaining this correction by fusing the spine. To do so, the spine is accessed using either an anterior approach through the chest or abdomen or a posterior longitudinal incision along the midline of the spine (i.e. posterior spinal correction and fusion surgery, PSF). The latter is considered the optimal technique for most patients [40]. When adequate exposure of the spine is achieved, spinal releases can be performed to facilitate scoliosis correction. This can include (a combination of) removal of the supraspinous and intraspinous ligaments, the facet joints or, in case of very severe deformities, the rib(heads) [45–47]. A popular osteotomy is that described by Ponte, who combined the sequential removal of the supraspinous and intraspinous ligaments, superior and inferior facet joints, flaval ligament, and part of the laminae [48]. Next, spinal anchor points are placed. These can either be screws, wires, hooks, bands, or a hybrid construct based on a combination of the afore mentioned. The spinal anchors are then connected using metal rods and corrective forces are applied to the instrumentation to correct the deformity. The lamina, transverse processes and facet joints are decorticated and bone graft is applied to induce a bony fusion. The rigid spinal instrumentation retains the correction during the first months after surgery. During this time the spinal fusion can mature to a stable bone mass and the scoliosis correction is maintained.

Operative treatment – outcome
During the last decades several technological advances have provided increased correction rates [49]. With the advent of pedicle screw based systems surgeons were able to correct the lateral curvature and rotation of the spine while having control over sagittal alignment for the first time. Patients report good scores on quality of life domains such as mental health, cosmetic appearance and satisfaction with treatment in the mid-term follow-up after surgery [50]. However, scoliosis surgery has remained an invasive endeavour. In PSF surgery the spine is accessed by a long incision across the back leaving the adolescent patients with a large scar for the rest of their lives. Intra-operative blood losses of more than 1.000 ml are not uncommon and a significant amount of the patients require a blood transfusion [51]. Average length of stay after surgery is about four or five days. To maintain curve correction the operated part of spine is fused, which has a detrimental effect on overall spinal mobility. Combined with the use of a substantial number of highly priced implants, scoliosis surgery is still an invasive and costly endeavour [52].

For a long time it was assumed that, if left untreated and progressed into adulthood, AIS would result in disabling pain, serious cardiopulmonary dysfunction, decreased rates of marriage, and increased unemployment and mortality rates [53–55]. This grim future justified the use of invasive surgical treatment. Later studies of better design demonstrated the problems of leaving the deformity untreated are less life-threatening, but rather encompass...
dissatisfaction with cosmetic appearance, increased prevalence of pain, and limitations of physical activity [8–11]. Additionally, with patients, parents, and surgeons focusing more and more on cosmetic outcome and quick recovery, it is important to improve current techniques and provide less invasive treatment options [50,56].

Negative effects of PSF surgery on physical function and activity are reported in comparison to non-surgically treated control groups. But, although significant, these effects are relatively mild considering the surgical trauma [9,57,58]. In particular, a physical activity in daily life such as walking shows only slight alterations [59–63]. This is extraordinary when the presumed key role of the spine during walking is taken into account: the spine is considered to function as a shock absorber, the engine that drives the pelvis, and a reducer of energy consumption during gait [64–66]. Thus, looking at it from a biomechanical point of view, the dissection of the paraspinal muscles and fusion of a large part of the spine during scoliosis surgery is expected to have a negative effect on gait. Compensatory mechanisms could obscure this negative effect and limit the measurable effect of surgery on gait parameters. Such mechanisms were previously demonstrated in patients treated with spinal braces or those suffering from lumbar disc herniations [67,68].

A substantial number of the patients return to sports at a lower level or do not engage in sports at all after surgery and the overall level of physical performance is reported to be lower than healthy controls [69]. Not only does fusion surgery result in an immediate negative effect, studies on the effect on long-term patient reported outcomes show a small, but statistically significant, decrease in physical function and activity after surgery compared to controls [9,57,58,70]. Moreover, there are concerns for long-term negative effects secondary to the fusion. One of these is adjacent segment degeneration (ASD), which refers to the advanced aging of the spinal segment proximal or distal to the fusion mass. It is often hypothesized that increases in adjacent segment motion induce stress and subsequently ASD [71–73]. Later in life ASD could play a role in low back pain [74–76]. In general it is agreed that the fusion length should be minimized to preserve as much mobile spinal segments as possible. Another negative side effect observed after scoliosis surgery is proximal junctional kyphosis, defined as an increased spinal kyphosis directly cephalad to the fusion. When a threshold of >10° kyphosis is used the incidence ranges from 7–35% [77]. This can in turn induce an increase in lordosis, which is a potential risk factor for facet joint degeneration [78,79].

To overcome the downsides associated with PSF surgery, the currently applied surgical techniques should be evaluated. In recent years the focus on obtaining a good sagittal alignment has increased [80]. Also, the effect of the surgical techniques on deformity correction and cosmetic outcome has been of great interest [81]. The use of intra-operative spinal releases in obtaining sufficient correction is controversial as results vary between studies. PSF surgery with Ponte osteotomies (i.e. removal of the supraspinous and intraspinous ligaments, the facet joints, flaval ligament, and part of the laminae) was previously compared to surgery with only removal of the ligaments and inferior facet joint in patients [82]. The Ponte osteotomies did not result in better deformity correction [82]. In contrast, others did observe improved correction rates when performing Ponte osteotomies [83]. Also, osteotomies significantly increase blood loss and operative time [51,82].

Besides improving currently used techniques, we should look into more substantial changes. Less invasive and fusionless techniques are thought to be the next step in the surgical treatment of AIS. Most of these fusionless techniques have been developed to modify growth in young patients <10 years of age. Examples are posterior growing rods, anterior vertebral body stapling, and vertebral body tethering [84–93]. Although promising results have been published, vertebral stapling and tethering of the vertebrae require a high degree of technical skill from the surgeon. These anterior implants are thought to reduce growth on the convexity of the curve and, by allowing growth on the concavity, the curve can correct during the growth of the patient. However, the patient needs to be skeletally immature as a significant degree of remaining growth is required for the surgery to be successful [88,91,93]. Since many countries do not engage in screening programs for scoliosis, numerous patients are referred to a specialized spine surgeon when the curve is already significant and the patient is lacking sufficient remaining growth [94]. This means current fusionless techniques are unavailable for most AIS patients.

In summary, AIS is a three-dimensional deformity that negatively affects the quality of life. Severe deformities require surgical correction, but current fusion-based techniques are time consuming, invasive, result in substantial blood loss, and leave the patient with a stiffened spine and a long scar. Fusion results in a permanent loss of spinal motion, reduced postoperative physical activity, and possible long-term complications such as ASD which can play a role in the occurrence of back pain. As such, there is room for improvement in the surgical treatment of patients suffering from AIS.
This thesis

In the foregoing it was illustrated that despite great advances over the past decades and a substantial body of research, there are still relevant questions regarding the techniques used during PSF surgery and the effect of fusion on outcomes such as physical function in daily life. Moreover, less-invasive and fusionless scoliosis surgery can potentially provide advantages over current techniques. Therefore, part I of this thesis aims to improve our understanding of the effect of PSF surgery on in vitro and in vivo biomechanics. The aim of part II is to evaluate a new fusionless surgical technique for the treatment of AIS. The specific research questions in this thesis are described below.

PART I

I. What is the effect on intra-operative spinal flexibility of posterior spinal releases?
Intra-operative ligament and facet joint releases are performed to make the spine more flexible to facilitate correction of the deformity. Evidence on clinical efficacy is contradicting, while these releases substantially contribute to intraoperative blood loss and duration of surgery, and pose a potential risk of neurological injury. Despite these substantial drawbacks, little is known about the contribution of the individual posterior spinal elements to spinal flexibility [95–99]. To shed more light on this problem, in Chapter 2 the impact of different intra-operative spinal releases on spinal flexibility is quantified in cadaveric spines.

II. What is the effect on the biomechanical properties of the human spine of a new embalming method, impacting our evaluation of new techniques for spinal surgery?
Similar to the research presented in chapter Chapter 2, in vitro experiments to evaluate new techniques for spinal surgery are often performed on spinal specimens that have not been embalmed (often referred to as ‘fresh frozen’). However, the accompanied risk of transfer of pathogens from the specimen to the researcher is a significant downside and the specimen can only be used for a restricted amount of time before the tissue deteriorates. A novel embalming method, Fix for Life (F4L), has previously been designed to remove pathogens from the specimen and prevent tissue deterioration, while leaving the biomechanical parameters unaltered. In Chapter 3 the effect of this embalming method on the biomechanical properties of human spinal specimens was quantified.

III. What mechanisms do patients with AIS utilise during gait to compensate for the loss of spinal motion after spinal correction and fusion surgery?
Considering the invasiveness of PSF surgery, the AIS patients recover relatively well [100–102]. This is remarkable as the spine is considered to play a vital role during everyday activities [64–66]. It is often hypothesized that increased motions in the unfused part of the spine or elsewhere in the body occur to compensate for the loss of motion at the levels of the fusion. However, actual scientific evidence for this hypothesis is lacking. Insights on the effect of fusion
could give us the possibly to understand and possibly treat short-term effects such as decreased postoperative physical function and activity [9,57,58,69,70]. Also, it could provide an explanation why long-term effects such as adjacent segment degeneration occur [71–77]. Chapter 4 presents the results of a gait analysis before and after scoliosis surgery to identify possible compensatory mechanisms in the lower limbs. In Chapter 5 possible compensatory increased motions in the adjacent unfused spinal segments were investigated. Lastly, in Chapter 6 a study on the possible compensatory motions of the shoulders in relation to the trunk is presented.

PART II

IV. What steps are needed when introducing a new medical technology into daily clinical practice?

With the ever-increasing development of new medical techniques and implants the physician must play an increasingly important role to select those that create a true increase in quality of care for the patient. With new technologies come associated risks and the latter is often an objection for many physicians to use a new technology. While this can avoid safety problems, it can also reduce the rate of healthcare improvements. In part II of this thesis a new technique for fusionless scoliosis correction was analysed that can potentially overcome the negative effects associated to PSF surgery. In Chapter 7 a case study, based on this new technique, is presented to illustrate how new medical technologies can be introduced into clinical practice within the Dutch healthcare system.

V. How does a novel periapical concave distraction device for the fusionless surgical correction of AIS affect spinal biomechanical properties?

Recently, a new and potentially less-invasive implant for fusionless scoliosis surgery was developed. In theory this fusionless technique has potential advantages over regular PSF surgery by preservation of spinal motion, but the actual effect on spinal biomechanics is unknown. Therefore, in Chapter 8 we performed an in vitro biomechanical study of the new implant.

VI. How effective and safe is the novel periapical concave distraction device for the fusionless surgical correction of AIS?

Besides the advantages of not requiring fusion, the new device also potentially decreases the length of the incision, amount of blood loss, duration of surgery and postoperative recovery period. However, the clinical effects and potential complications are yet unknown. Therefore, based on the results presented in Chapter 7 and Chapter 8, a prospective cohort study in a selected patient group was initiated. In Chapter 9 the preliminary clinical results are presented.

Finally, in Chapter 10, a general discussion of the work performed for this thesis is presented. There, the results of the laboratory and clinical studies are summarized. Their impact is reviewed and related to current theories on spinal biomechanics and outcomes after AIS surgery, resulting in recommendations on the future treatment of AIS and concluding remarks.
References


