

# From the Wild West to the Moon: The Future of Early Onset Scoliosis

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## Introduction

Here is a million-dollar question: What does the landscape look like for Early Onset Scoliosis (EOS) in the future? The reasons we love taking care of children with EOS are the same reasons that question is so difficult to answer.

Most of us who take care of EOS also take care of kids with adolescent idiopathic scoliosis (AIS). While surgeons will often have slightly different techniques and may get in heated debates about stopping at T12 vs. L1, our overall treatment approach to deformity correction in AIS is *relatively* consistent. Also, while we have undoubtedly improved our understanding of treatment techniques and outcomes in AIS, the needle has not moved dramatically with regards to implant technology, surgical technique, or patient outcomes in AIS surgery over the last 5–10 years.

In stark contrast, when you think about the treatment options used to treat EOS, as Claire Cook has been quoted, “If plan A doesn’t work, the alphabet has 25 more letters—204 if you are in Japan.” Patients with EOS have incredible diversity in underlying etiology, expected growth rates, clinical presentation, and severity of disease. We have a diverse arsenal of nonsurgical and surgical techniques that are applied to different populations variably. All of our treatment options are associated with high complication rates, and those complication rates have not changed much over time. We do not fully understand the natural history between treatment methods, and it is difficult to compare treatment groups to appropriate control populations. We have a number of

outcome measures that may reflect our successes or failures, but we have a poor understanding of how they relate to one another, they may be difficult to obtain in this population, and it is unclear which outcome measures are the “best.”

While this complexity and uncertainty can be frustrating at its worse and exhilarating at its best, it does explain the rapid evolution of the approach to EOS over the last 10 years. Many of us attend the International Congress of Early Onset Scoliosis, and the size and focus of that meeting is truly dynamic each and every year. It has grown and matured immensely, and what it is today is nothing like it was 10 years ago. I fully anticipate 10 years from now it will be completely different and will be focusing on topics that we cannot yet envision. Despite the vast amount we have learned about EOS, there is so much that we don’t know which makes the future so interesting (and uncertain).

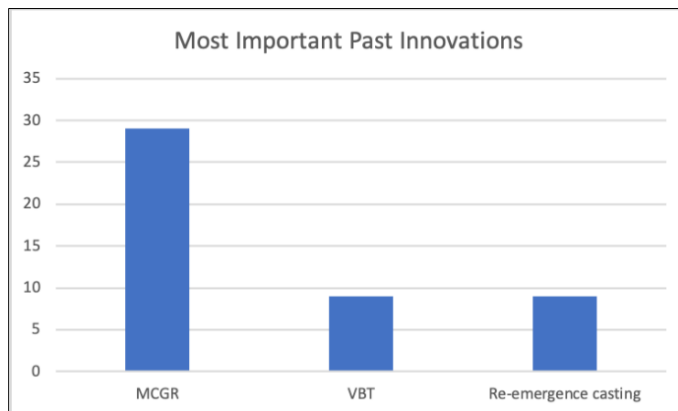
In putting this manuscript together, I polled the leadership of the Pediatric Spine Study Group (PSSG) and PSSG membership regarding their thoughts on the future direction of EOS treatment. Fifty-nine members responded, with 44 having more than 10 years of EOS experience and the remaining 15 respondents with 5–15 years of experience. The variability in the responses of this group of very experienced surgeons reflects the complexity and variability in the treatment of EOS at our current state. I don’t think anyone can predict what will happen in this space in the future, but I hope to highlight some themes

that will undoubtedly be at the forefront of our efforts to better understand the diagnosis, natural history, treatment, and treatment outcomes of EOS.

## Survey Response/Interpretation

### *What Have Been the Important Advancements in the Treatment of EOS?*

I think the first step in understanding what the future may look like is to understand what significant advances have been made in EOS. Members of the PSSG were asked, “*What has been the most surprising innovation/advancement you did not anticipate in EOS over the last 10 years?*” It is not surprising, given the number of implant innovations that have occurred, that the overwhelming majority noted specific implants or techniques (Magnetically Controlled Growing Rods (MCGR), Vertebral Body Tethering (VBT), casting) as the most important innovations.



It is hard to argue against Magnetically Controlled Growing Rods (MCGR) being the most common response. It really changed how we approached EOS and had incredible promise in limiting anesthetics through noninvasive lengthening’s. While the majority felt that the most significant advancement was the development of MCGR, it is interesting that many also noted the failure of MCGR to live up to its potential as the most surprising development. While the MCGR implant certainly is an “upgrade” in its ability to reduce planned lengthening operations, it is still associated with junctional kyphosis, failure to lengthen, and complications that lead to similar rates of unplanned return to the operating room (UPROR) to

other growth-friendly implants.<sup>1-3</sup> They are also associated with high cost,<sup>4,5</sup> and conversions from traditional growing constructs do not do as well.<sup>6</sup> Its size and its design necessitate a long straight section of implant which can make it problematic in those patients with poor soft tissue, small size, and pre-existing kyphosis. While it does provide a lot of benefits, it unfortunately does not solve many issues surrounding the underlying patients’ disease state or severity.

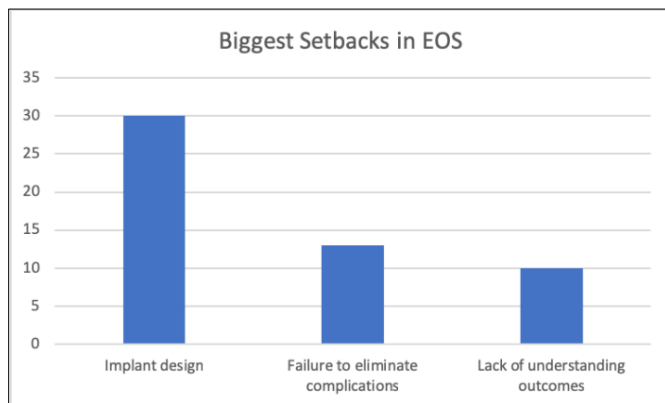
If we were to ask this question 2–3 years from now, you might find a shift with more commonly choosing vertebral body tethering (VBT) as the most important innovation.<sup>7</sup> However, the discussion will likely be the same in that while it offers some advantages in its ability to maintain motion and harness growth to assist in correction, it shares a higher-than-expected complication rate. We have yet to find the “holy grail” in implant design. Vertical Expandable Prosthetic Titanium Rib (VEPTR™), Traditional Growing Rods (TGR), Growth Guidance/Shilla™, MCGR, and VBT all represent techniques that can help select populations of EOS, but all are far from perfect and share the same challenge of high complication rates.

Given the complication rates associated with all of these implant designs, I think it is important to point out that there has been a bit of a trend to narrow the age range where we use growth-friendly implants. On the front end, we know that the complication rates are higher the earlier you start growth-friendly treatment,<sup>8,9</sup> and there has been success in curing or delaying surgical treatment with less invasive options such as casting or bracing for EOS.<sup>10,11</sup> Therefore, there has been a trend to delay initiation of surgical treatment in EOS as long as possible. On the other end, there is some evidence that early fusion may lead to better correction and minimal loss of growth in “late” EOS.<sup>12</sup> For this reason, some respondents pointed out the trend toward fusion of “tweeners” rather than primary implantation of growth-friendly implants. This narrowed window reflects our current struggle with imperfect implants associated with high complication rates.

*What Have Been the Important Setbacks in the Treatment of EOS?*

As Edmund Burke has been quoted, “Those who don’t know history are destined to repeat it.” As discussed, the complication rates associated with all types of treatment of EOS are high. However, our ability to advance into the future is highly dependent on our ability to adapt and learn from our past experiences. PSSG members were polled, “*What do you feel have been the greatest failures/setbacks/disappointments over the last 10 years in EOS?*” The results here mirror the responses to the greatest advancements discussed above. This is likely because every advancement has not been perfect and is associated with some disappointment.

The results here are again dominated by implant-related issues, with many pointing out specific issues with implant design and complication risk. Most feel that we still have not found the right design. This failure is related to the fact that with implant advancement, complication rates and UPROR rates have remained fairly constant. Specific examples cited include failure to lengthen, metallosis, crankshaft, kyphosis, adjacent deformity, autofusion, and infection.



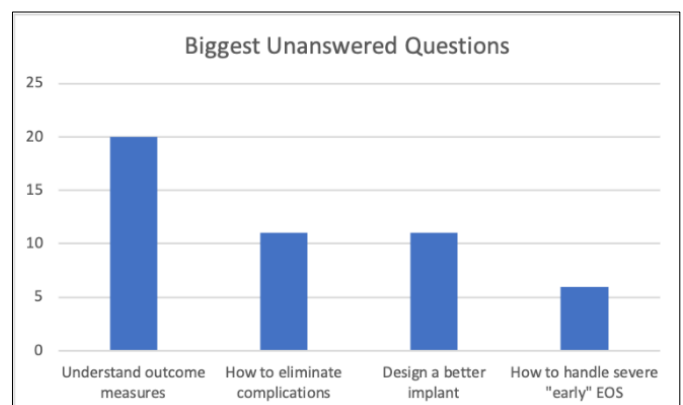
However, the answers to this question did demonstrate an important shift that will be addressed later as we discuss the future of EOS. Respondents began identifying that we don’t have a good understanding of appropriate outcomes to measure, nor do we understand if we are changing the natural history with treatment. While strides have been made in our ability to look at outcomes in this population with the development of

questionnaires like the EOSQ,<sup>13,14</sup> we don’t have a good understanding of concepts such as minimal clinically important difference (MCID) in this population, nor do we have appropriate disability adjusted life years (DALYs) for children as examples. As we look to the future in subsequent sections, an understanding of outcome measures is going to be critically important in the future advancement of treatment for EOS.

I also want to point out one other comment that may be thought provoking/controversial but worth mention. One respondent discussed the allegiance of surgeons to a single approach as the biggest disappointment in our treatment of EOS. I think that there may be some truth to this as will also be discussed in future sections. All of these techniques are part of a toolbox that we have to approach a complex disease affecting a diverse population of individuals. It is likely that different techniques are needed for different individuals and deformity types, and there is likely not going to be a “holy grail” that will be able to be applied universally across all patients.

*What Do We Need to Answer Next?*

In recognizing our past struggles, I queried the PSSG, “*What is the most important unanswered struggle/challenge in EOS that you would like answered in the next 10 years?*” In phrasing it this way, I was trying to get at some of the non-implant innovation/understanding that is needed as we move into the future. Many responded with similar implant-related answers based on our historical challenges. Eliminating complications and designing a better implant to do so are clearly still unanswered questions.



However, I was pleased to see a progressive trend in an increased desire to understand outcome measures. Several would like to know how to handle severe “early” EOS, asking questions such as, “When do we start treatment?”, but most feel that we do not understand outcomes related to underlying disease or the effect our treatment has on EOS. For me, this is an important inflection point because I do not think we will ever design a better implant without better comprehension of some of these core principles. The table below is a snapshot of the types of critical, basic questions that remain unanswered with regard to understanding underlying disease state, how it compares to “normal,” and the potential impact (or lack of impact) treatment may have on core clinical and patient-focused outcomes.

<b>Common Outcome Questions in EOS</b>
What is normal spine growth?
Are we improving lung function?
How do we know it is working?
Are we changing the natural history?
Are we improving Quality of Life (QOL)
How does deformity/pulmonary function relate to QOL?

The reality is that we have a complex diverse population with regard to underlying cause and curve characteristics.<sup>15</sup> Patients are spread across a wide age range, and we are treating them during a rapid period of trunk and lung growth.<sup>16</sup> Even at different life stages, patients have different individual growth rates that also vary by underlying diagnosis.<sup>17,18</sup> Surgeons who take care of patients with EOS have variable indications, timing, technique, and execution.

The most commonly reported outcomes are those that are universally available and easily measured. Most EOS research has historically reported 2D measurements such as spinal length. However, these 2D measurements correlate poorly with pulmonary function tests (PFTs).<sup>19</sup> Ultimately, while we want to make sure the spine grows with our treatment, the real outcome we are trying to achieve is improved pulmonary function. Unfortunately, due to age or medical conditions, PFTs are difficult to obtain in

the EOS population as there are challenges with regard to cooperation, effort, and technique.<sup>20</sup> Three-dimensional measurements can be made but do not capture the dynamic nature of lung function.<sup>21</sup>

Dynamic MRI<sup>22,23</sup> and surrogates such as elevated hemoglobin<sup>24,25</sup> have limitations and cannot be used universally. Patient-related function and outcome measures such as EOSQ,<sup>14,26</sup> the 6-minute walk test,<sup>27</sup> and Activities Scale for Kids performance<sup>28</sup> are available but are still in their infancy with regard to our understanding of how they relate to success/failure of our EOS treatment. So currently we have, at best, a bunch of surrogates to measure how we are doing. We know that we are making kids different with treatment (taller, straighter), but we still are searching for outcome measures that prove that we are making a meaningful difference on pulmonary function and functional outcomes for these children. Without identifying the right outcome measures, we will continue to struggle to find the right treatment solutions for patients with EOS.

*What May Be on the Horizon?*

While it is difficult to anticipate what technological advancements may occur, most would agree that finding the “holy grail” implant that could be noninvasively lengthened without complications would be on their top of the list. To get a sense of a look into the future, PSSG members were asked, “*What is the most outside the box innovation/advancement you could imagine*”

<b>“Outside the Box” Implant Innovations for EOS</b>
Curved actuator
Hydraulic Implants
Self-propelling growing rods
Smart implants (on/off, measure growth)
Remote monitoring/control of implant stress/force
Tether that can be tensioned/released with an external device
Stable anchors with better fixation to bone
Smaller, fatigue resistant implants
Custom, modifiable correction (Illizarov type principles)

<b>“Outside the Box” Non-implant Innovations for EOS</b>
Magnetic signaling of the vertebral growth plates
Biologics/Growth plate injections to induce/inhibit growth
Vascular stimulation
Radiofrequency to influence growth plate
Gene therapy

*occurring in EOS in the future?”* Many identified changes to current growth-friendly systems. Some pointed to increased use of enabling technology such as robotics to improve implant placement and construct design. Whereas I had expected that the majority of ideas would surround implant design, a surprising number of respondents had ideas that deviated away from the traditional way we have thought about surgery for EOS in the past.

There was a clear emphasis on having a better understanding of the underlying cause and disease process to treat EOS. There was a focus on predictive analytics and outcomes and the use of existing technology such as dynamic MRI or wearable technology to assess function to create patient-specific treatment. Having a better understanding of nonoperative care with casting and bracing is a key component to our success.

What is most interesting looking forward is that we are starting to shift the way we have traditionally thought about treatment (driven by implant design). Many are beginning to ask, “Is there a way to correct or influence growth *without* implants?” A large number of PSSG members imagine a future world where we can modulate spinal growth without surgery or implants. This clearly requires us to understand the genetics and biologic etiology of the underlying disease as well as the natural history. If you could understand what was driving the disease and its progression, then you could attack the root cause rather than respond secondarily with surgery.

## Conclusion

So, back to the million (or billion) dollar question: What does the landscape look like for EOS in the future? I don’t think any of us really know. I think there are certain things that we can imagine and realize while some things will likely remain hopeful dreams for a while. It makes taking care of kids with EOS exciting and will continue to satisfy our inquisitive minds as we craft research that will move us into the future of EOS.

What is clear is that we lack a perfect implant. But I am not sure that the search for the perfect implant is what we need or what the future will look like. There will undoubtedly be new designs and new techniques that emerge. Certainly, it is not hard to imagine sensors and technology that will improve our ability to monitor/measure mechanical properties of growth-friendly implants noninvasively. I am confident that improvements in metallurgy will improve profile and strength of implants in patients that require less bulky solutions.

It is unlikely that there is a “holy grail.” Allegiance to a single implant is unlikely to satisfy the complex needs of this population. EOS patients are diverse and therefore require diverse treatment solutions. We will have a toolbox (Casting, Bracing, Vertical Expandable Prosthetic Titanium Rib (VEPTR™), Traditional Growing Rods (TGR), Growth Guidance/Shilla™, MCGR, VBT, and others). The tools in this toolbox may be appropriate for different patients in different situations. We will gain a better understanding of how these various tools perform with unique patients and patient-specific treatment based on predictive analytics will help drive our decision-making.

I believe that our focus has been on the what or the how. Our innovation in the treatment of EOS has largely focused on implant development. I don’t think we have had any other choice, but this is inherently a reactive strategy. We are secondarily treating the sequela of a disease we poorly understand. However, the strides we have made are immense when you consider the innovation we have experienced over the last 10–15 years with

regard to implant design and strategy. Undoubtedly, continued innovation in surgical technique will continue to be a crucial component to our short-, mid-, and long-term success. In all probability, the most achievable and noticeable progress will be made with innovation of surgical implants and technique.

However, the key to the future will require a paradigm shift from the what and how to the who, when, and why. In order to have a more proactive approach to EOS treatment, we need to have a better understanding of an individual patient's disease process. What is causing it? What is their predicted growth? What will happen to their curve over time? This will open doors to nontraditional treatment options discussed above where we attack the root cause of the problem before we are forced to employ treatment aimed to control a curve that has already progressed. Understanding cause/biology/genetics will allow us to better understand when we should employ different treatment strategies. But as important as it is to understand underlying etiology and cause, we also need to know why we are treating these children and if we are making a difference in their outcomes. A clear focus on defining and understanding the right outcome measures is the only way to understand the differential impact of various treatment strategies on EOS patient populations. I anticipate increased efforts to define our successes and failures with an improved understanding of which outcome measures best capture our patients' functional outcomes and quality of life.

Despite a lack of clarity in the future of our field, I do know a few things that will be an absolute certainty going forward. Those of us who take care of children with EOS will (1) provide the compassionate, quality-focused care, (2) strive to maximize outcomes and improve quality of life, (3) be intellectually stimulated every day, (4) learn from expected setbacks and use them to adapt and move forward, and (5) continually challenge and push each other to innovate and advance our understanding and treatment of EOS.

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