

Guest Editorial Retina and Uvea

## Implementation of a robotic surgical system in gene therapy – A way forward

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Gene therapy and robotic surgery are innovative medical technologies. They address different aspects of medical treatment. The goals of implementing these technologies together are to improve patient outcomes and quality of life. Gene therapy is focused on treating the underlying genetic causes of disease, while robotic surgery is focused on improving surgical precision and reducing the invasiveness of surgical procedures.<sup>[1]</sup> Gene therapy is a medical technique that works by altering the genetic material of a patient's cells by recovering the function of the cells to treat or prevent disease. This can be done by embedding new genes into the patient's cells, replacing or repairing the pre-existing gene mutation. On the other hand, robotic surgery is a safer and minimally invasive surgical technique that involves the use of robotic arms to perform various surgical procedures. This can provide greater precision and control to the surgeon, leading to better outcomes for patients. Implementation of robotic surgery has become routine in multiple surgical arenas such as urology, gynecology, ophthalmology, prostatectomies, cardiac valve repair, etc. Increased maneuverability, better precision, and excellent visualization over traditionally performed surgical procedures have resulted in the amalgamation of robotic surgery into operating theaters in many surgical fields. The Da Vinci surgical system (Intuitive Surgical, Inc.) had been the most predominant, commercially available system in the past two decades, with an installed base of over 4000 units globally.<sup>[2]</sup> It was authorized by Food and Drug Administration in 2000 for surgeries in adults as well as pediatrics. The system is used in laparoscopic surgery, non-cardiovascular thoracoscopy, gynecologic intervention, thoroscopically assisted cardiotomy, and urologic surgical procedures.<sup>[2,3]</sup>

Nowadays, gene therapy is advancing rapidly worldwide. Although in India, we still do not have the advances in gene therapy. Luxturna gene therapy is trending for the treatment of retinal pigment epithelium 65 (RPE65) gene-associated retinal dystrophy. RPE65 protein is produced at the back of the eye in the outermost layer of retina called RPE, which is an essential protein in maintaining a normal visual cycle. Alterations in the RPE65 gene lead to vision loss due to the loss of function of RPE cells. It is a progressive degeneration of the photoreceptor cells of the retina. It is found that the mutation in the RPE65 gene is one of the major causes of leber congenital amaurosis. The prominent symptom of this condition usually starts with delayed dark adaptation and difficulty in dim light or night vision in early childhood.<sup>[1]</sup> In the United Kingdom, patients with RPE65-associated disease are being treated with the luxturna gene therapy under the National Health Service.<sup>[4]</sup> Luxturna contains the active substance voretigene neparvovec which is given as a single dose of injection in the subretinal space. Gene delivery through subretinal injection is a delicate procedure to perform, as it requires precise targeting of the subretinal space, without

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going too deep. Reflux-free delivery in the subretinal space is essential to make it more effective and safer which is possible with the help of robotic arms-assisted surgery.<sup>[5]</sup> Preceyes B.V. is a medical robotics company that is currently in use for vitreo retinal surgeries. A study was conducted by Ladha *et al.* using Preceyes surgical system model R0 (Preceyes BV, Eindhoven, the Netherlands) which showed the advantages of robotic assistance in simulated subretinal injection and its significance for gene therapy over manual approach.<sup>[5]</sup>

“Very few surgeons are trained to do this and reflux has been shown to occur in virtually all cases with Luxturna, which means that 30–50% of the amount is dispersed into the vitreous. The challenges of subretinal delivery have so far been a hurdle in the way of drug development,” de Smet said.<sup>[6]</sup>

While gene therapy and robotic surgery are both cutting-edge medical technologies, they address different aspects of medical treatment. Gene therapy is focused on treating the underlying genetic causes of disease and robotic surgery is focused on improving surgical precision and reducing the invasiveness of surgical procedures. Robotic surgery is a fancy surgery that utilizes robotic arms controlled by a surgeon to perform complex and delicate procedures. It provides greater precision, control, higher maneuverability, and steadiness for target-oriented surgeries than traditional surgeries.<sup>[7]</sup> With its precision, it allows a great number of ophthalmic surgeons with proper training to perform the complicated gene delivery in the subretinal space safely and minimize the reflux into the vitreous cavity during the procedure, and inject the perfect amount of drug in the perfect place. The precision and steadiness that are required during the subretinal delivery of the drug are well served by the use of robotic arms. It reduces tremors that occur when the drug is administered manually. It assists the surgeon in performing the desired subretinal delivery with steadiness and without moving away from the site of injection after reaching there.

In conclusion, robotic surgery has revolutionized the field of surgery and has become a game-changer in the way that many procedures are performed. “A human cannot hold the tip of a tool steady inside a blood micro vessel for several minutes, but a robot can,” said Dr. Gehlbach.<sup>[8]</sup>

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