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#### **Review article**

#### Title: Hydrogel-based Drug Delivery for Tissue Engineering

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#### Abstract

Tissue engineering is a multidisciplinary field that aims to restore, maintain, and improve tissue performance by producing functional tissue constructs. The three major domains of tissue engineering are isolated cells or stem cells, biomaterial scaffolds and biomolecules. Hydrogels are commonly studied as scaffold materials for tissue regeneration due to its unique characteristics, i.e., excellent water absorbing and swelling capacity, tunable mechanical properties, porous structure, biocompatibility, biodegradability, flexibility similar to natural tissues and responsive to various stimuli (e.g., changes in pH, humidity, light and temperature). In the past decades, additive manufacturing (bioprinting) has emerged as a powerful technology in tissue and organ regeneration where it incorporates hydrogels as functional scaffolds. Various hydrogel-based delivery systems have also been developed in search of ideal scaffold for tissue engineering. In view of the potential of hydrogels in the field of tissue engineering, herein presents a review focusing on application of hydrogels for drug delivery in tissue engineering as well as additive manufacturing.

Keywords: bioprinting, hydrogels, smart hydrogels, tissue engineering, tissue repair and regeneration

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#### Introduction

Tissue engineering is a multidisciplinary field that aims to restore, maintain, and improve tissue performance by producing functional tissue constructs. In view of the limitations of current medical therapies for tissue injuries and shortage of transplantable organs, tissue engineering is regarded as the solution to these issues and has been explored extensively. Tissue engineering consists of three major components i.e., isolated cells or stem cells of the tissue of interest, biomaterial scaffolds, and biomolecules which are necessary for cellular development. <sup>1</sup>

Biomaterial scaffold is crucial for successful tissue engineering as it mimics the native extracellular matrices (ECM) to promote cell function, adhesion and tissue transplantation. Among the variety of biomaterial, hydrogels are widely used to fabricate scaffolds for tissue regeneration. Hydrogels are three-dimensional cross-linked polymeric networks with excellent water absorbing and swelling capacity while remain insoluble in the physiological environment. Other unique properties of hydrogels – excellent and modifiable mechanical properties, porous structure, biocompatibility, biodegradability, flexibility similar to natural tissues, responsive to various stimuli (e.g., changes in pH, humidity, light and temperature) – made it a promising candidate for tissue engineering. <sup>2</sup> To date, the application of hydrogel can be viewed in various tissue engineering and new advancements have been explored constantly to expand its applications in different tissue repair.



Figure 1. Commonly employed mechanism of tissue engineering.<sup>1</sup>

# **Characteristics of Hydrogel as Scaffold**

Hydrogel is characterised with three-dimensional polymeric networks that is capable of absorbing substantial amounts of water and swells, while remaining insoluble in water and body fluid. The tremendous water absorption capacity of hydrogel is attributed to the hydrophilic side chain on the polymeric backbone while the dynamic cross-links between polymer chains maintain the integrity of the hydrogel network therefore resistant to dissolution. <sup>2</sup> Furthermore, hydrogel possess flexibility similar to the natural ECM to support the adhesion, engraftation, survival and proliferation of the neighbouring cells. <sup>2</sup>

Moreover, hydrogel is reasonably deformable and adaptive to the type of surface to which

they are applied, when combined with the bio-mucoadhesive nature of hydrogels can be utilised to confine them at the site of tissue injuries.<sup>3</sup>

Porosity is another critical property that permits the use of hydrogel in tissue engineering. Together with the high swelling structure, the interconnecting pores enable transfer of gases, nutrients, cell metabolites, and waste as well as assisting neovascularization to support growth of cells. <sup>1</sup> On top of that, the porous nature provides space for entrapment of biomolecules thus being utilised as carriers in sustained drug delivery system. <sup>4</sup>

An ideal scaffold should degrade in the later stage of tissue development to avoid hindering the complete tissue growth and confer a negligible inflammation extent. In view of these considerations, biodegradable and biocompatible hydrogels are therefore apt for tissue scaffold. <sup>3</sup> The mechanical properties of hydrogel can be tailored through modification of cross-linking of the polymer matrix, renders it to be modified for different tissue generation that normally demand different properties and functions of scaffolds. <sup>1,2</sup> Moreover, hydrogels can be made to respond to external stimuli by changing its mechanical structure. <sup>3</sup> The stimuli may be physical such as temperature, humidity and magnetic field, or chemical which include pH, ions and glucose. <sup>2</sup>

#### Hydrogels in Tissue Regeneration Technology

There are many tissue regeneration technologies being studied, among which, additive manufacturing utilises hydrogels to fabricate functional scaffolds.

# Hydrogel for Three-Dimensional Bioprinting

Three-dimensional (3D) printing, also known as additive manufacturing, is a technology of building tissues or organs to reconstruct or replace damaged or defect tissues and organs. <sup>5</sup> The mechanism of 3D printing involved construction of tissue or organs layer-by-layer using a bottoms-up approach, guided by the computer model of the specific tissue or organ. 3D printings offer the unique advantages for tissue engineering as it can be customised to constructing tissues or organs with high structural complexity and is patient-specific. <sup>5</sup>

There are various 3D printing methods available currently, among which, bioprinting utilises hydrogel as bio-ink for the printing of tissue constructs. Hydrogel are highly preferred for 3D culture due to their printable, cross-linkable, biocompatible nature and high swelling capacity.

<sup>5</sup> In addition, the cells and other biological molecules can be mixed with bio-inks in the printing step thus creating a cell-encapsulated scaffold. Due to the combined advantages of 3D printing and hydrogel, 3D bioprinting has gained tremendous attention to generate 3D cell culture for tissue engineering. Recently, Tijore et al. <sup>6</sup> proved that the 3D bioprinted microchanneled gelatin hydrogel induced myocardial differentiation of stem cells and promoted the growth of cardiomyocytes, suggesting the possibility of in vivo generation of cell constructs for cardiac tissue engineering.

#### Hydrogel for Four-Dimensional Bioprinting

Apart from 3D printing, four-dimensional (4D) bioprinting has emerged as a more advanced approach for tissue engineering. 4D bioprinting employs a similar mechanism and offers the same advantages of 3D bioprinting. The difference lies in the incorporation of intelligent materials (e.g., smart hydrogels) which allows a 4D cell culture to respond to various stimuli and adapt to the changing environment consequently providing optimal environment for tissue regeneration. When applied with minimally invasive procedures (i.e., injection method), the cell cultures may access to sites normally difficult to reach, <sup>5</sup> When arrived at the target site and exposed with the specific stimuli, the scaffolds undergo stimuli-induced structural change (i.e., swelling, shape change and self-assembly) to allow adhesion and subsequent cellular development.

With the emergence of 4D printing, researchers have begun to explore its potential in tissue engineering. Recently, Miao et al. <sup>7</sup> has fabricated 4D smart scaffolds that showed excellent cell compatibility as well as active differentiation of human bone marrow mesenchymal stem cell on the printed scaffolds, indicating its potential for cardiac tissue engineering.



**Figure 2.** (A) 3D and 4D printing technologies to fabricate scaffolds; (B) structural changes in smart materials with exposure of external stimuli.<sup>8</sup>

#### Advancements in Hydrogels-based Drug Delivery for Tissue Engineering

To date, hydrogel has been experimented over and over and different delivery systems have been developed to accommodate for the need of ideal scaffold. Here highlights a few hydrogel-based drug delivery approaches which demonstrate promising function for tissue engineering.

# Hydrogel-based Sustained Drug Released Systems

Tissue regenerations such as bone tissue repair and regeneration are complex and multiphasic processes that involve bioactive molecules of different levels. Hence, controlled sustained release of these bioactive components from the scaffolds has also been regarded as the key to create the optimal microenvironment and to achieve the desired tissue repair outcomes. In general, the drug release profile is highly dependent on parameters such as pore size, crosslinking density and degradation rate of the matrix. <sup>9</sup> As these parameters are manipulatable when designing hydrogel matrices, biomolecules can be formulated to have different release kinetics, i.e., in burst or controlled release.

Tremendous effort has been put into designing an ideal sustained-release system using hydrogel and plenty of research has demonstrated favourable results. These includes

controlled release of peptides (e.g., BMP) and growth factors (e.g., VGEF) <sup>10</sup>, parathyroid hormone <sup>11</sup> and miRNA <sup>12</sup> from hydrogel matrix in bone tissue engineering.

As inflammation and immune response are inevitable and may jeopardise bone regeneration, incorporation of immunomodulatory drugs into the scaffold together with cells and other biomolecules is viewed as a solution to this concern. Zhang et al. <sup>13</sup> who fabricated a tetra-PEG hydrogel-based aspirin sustained release system has demonstrated reduced local inflammation, indicating that incorporation of aspirin abates the inflammation during bone regeneration which benefits the bone repair process. <sup>13</sup>

#### Nanocomposite Hydrogels

Nanocomposite hydrogels involve the incorporation of nanomaterials into the threedimensional networks through physical or chemical crosslinking. The addition of nanoparticles is significant as it is capable of improving the physical and chemical properties of the scaffold, i.e., mechanical strength and toughness, protein and cell adhesiveness, elasticity, drug loading capacity, and degradation rate. <sup>14</sup> Various nanocomposite hydrogels have been developed to accommodate different functions for different tissue engineering (**Fig. 3**). For instance, Emami et al. <sup>15</sup> who fabricated a nanocomposite hydrogel based on gelatin/oxidised alginate has concluded incorporation of nanohydroxyapatite (nHA) provided self-healing property, high porosity, increased cytocompatibility, tunable gelling features in hydrogel for bone tissue regeneration.

Depending on the types of nanoparticles applied to the hydrogel network, additional and improved properties may be discovered from the nanocomposite hydrogels. An example depicting this is addition of zinc oxide nanoparticles (nZnO) into chitosan/gelatin hydrogel, the resultant hydrogel exhibits higher antimicrobial activity, lower cytotoxicity. <sup>16</sup> Such invention has showed great potential in skin tissue engineering as risk of infection is often concerned during skin repair and regeneration. As naproxen ionised at pH above 4.15, the positive charge of nZnO attracts the negatively charged drug molecules thus achieving a large load and continuous release of naproxen. <sup>16</sup>



**Figure 3.** Various nanocomposite hydrogels were developed and studied for different tissue engineering. <sup>14</sup>

# Stimuli-responsive hydrogels/ Smart hydrogels

Another notable characteristic of hydrogel is undoubtedly its ability to adapt by interchangeable sol-gel conditions which leads to the invention of smart hydrogel, also known as stimuli-responsive hydrogels (SRHs). Unlike conventional hydrogels, the design of smart hydrogel utilises surface-specific modification on polymer structure which allowing them to respond to various external stimuli. When exposed to the stimuli, the polymers react by changing the swelling behaviour, sol-gel transition, network structure, permeability, or mechanical strength. <sup>3</sup> Generally, smart hydrogels can be classified based on the stimuli and there are two broad categories of stimuli, i.e., physical and chemical stimuli. Examples of physical stimuli are temperature, magnetic fields, and humidity, while that of chemical stimuli includes pH and ions strength.

In the past decades, smart hydrogels have been extensively studied for the use in different

tissue regeneration. An example of smart hydrogels is the enzyme-mediated tissue adhesive hydrogels designed by Kim et al. <sup>17</sup> for meniscus repair of which tyrosinase was used to activate the tyrosine conjugated hyaluronic acid and gelatin hydrogels.

#### DNA-based Hydrogels

DNA-based hydrogel is a hybrid bionanomaterial developed from deoxyribosenucleic acid (DNA) and composed of cross-linked DNA chains in the 3D structure. In addition to the advantage confer by common hydrogel, DNA hydrogel preserves the biological features of DNA, i.e., sequence programmability, molecular recognition, excellent biocompatibility, and biodegradability. <sup>18</sup> As compared to traditional hydrogel, DNA-based hydrogels are superior in terms of self-assembly, programmable design and self-healing which is beneficial for cell migration. <sup>18</sup> In terms of encapsulation of cells, biomolecule and drugs, DNA-based hydrogels are capable of loading any other type of nucleic acid molecules (e.g., siRNA, miRNA) and DNA binding drugs as well as higher drug loading capacity. <sup>18</sup>

Moreover, DNA-hydrogel can be modified to be responsive to external stimuli, like smart hydrogels. The application of DNA-based hydrogels can be seen in various tissue engineering as well as tissue regeneration technology such as 3D bioprinting.

#### **Recent Clinical Trial**

In 2022, Niemeyer et al. <sup>19</sup> studied the treatment of large cartilage defects in the knee by hydrogel-based autologous chondrocyte implantation in a two-year, prospective, single arm, multicenter phase III trial involving 100 patients. The group had produced an albumin-hyaluronan-based hydrogel that is biocompatible and can be cross-linked in situ, to serve as a carrier in matrix-assisted autologous chondrocyte implantation (M-ACI). The administration of M-ACI was performed arthroscopically by NOVOCART® Injection plus. Due to the chondrocyte-loaded biomaterial's low viscosity and injectability, it encouraged homogenous cell distribution and excellent ingrowth of regenerated tissue into the defect bed. Moreover, the hydrogels were capable of preventing inflammatory and endothelial cell invasion, thus producing anti-inflammatory, anti-angiogenic, and thus also anti-osteogenic effects. <sup>19</sup>

The clinical outcome was assessed using the Knee Injury and Osteoarthritis Outcome Score (KOOS) on 3-, 6-, 12-, 18- and 24-months post operation (**Fig. 4**). Of which 93% of the patients score was at least 10 points higher, as early as 3 months after injection, indicating

significant improvement of the clinical symptoms. <sup>19</sup> Moreover, the repair tissue properties were assessed through Magnetic Resonance Observation of Cartilage Repair Tissue (MOCART) score and T2-mapping. <sup>19</sup> Both of which demonstrated progressive graft maturation and cartilage re-organization from 12 to 24 months suggesting minimal duration for the maturation of cartilage graft after ACI. <sup>19</sup>

Despite limitations in the research (e.g., lack of control group) and adverse reaction (e.g., arthralgia, joint swelling, and muscle dystrophy) of the formulation, the results still indicate the clinical significance of M-ACI with NOVOCART® Inject plus as a safe and efficacious treatment alternative for patients with large cartilage defects.<sup>19</sup>



**Figure 4.** Knee Injury and Osteoarthritis Outcome Score (KOOS) responder rate on 3-, 6-, 12-, 18- and 24-months post operation.<sup>19</sup>

# Conclusion

In view of the limitation of current medical and surgical interventions in treating severe tissue injuries, tissue engineering has been viewed as a promising alternative that attracts tremendous attention. To diversify the application of tissue engineering, hydrogel scaffolds that are characterised with tunable physicochemical properties have been experimented over different approaches, leading to new advancements with enhanced functions as mentioned above. The combination of different types of hydrogels with latest additive manufacturing technologies is also demonstrated in 3D and 4D bioprinting. A clinical trial on M-ACI for cartilage defects also demonstrated clinically significance improvement. Although challenges remained in designing a perfect scaffold for tissue engineering, it is certain that, with more research, tissue engineering holds great potential to dominate the medical care in the future.

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#### **Review article**

#### Implant Dentistry- Transitioning into a New Niche

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#### Abstract

Implant dentistry has grown leaps and bounds over decades and currently it is at an unprecedented peak. Especially this decade has witnessed huge leaps forward in techniques, technologies, materials, concepts and philosophies of implant treatment. In less than just a few decades, dental implants have moved from the fringes of dentistry to the mainstream. Indeed, dental implants are now utilized in situations not foreseen even a decade ago. We need to reflect on the many significant developments in dental implants technology which offer better and a more satisfying treatment option to our patients. This article reviews the merits of current technologies as well as throws light onto the future of the implant speciality.

Keywords: Dental Implants, Zirconia, Surgical Guides

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#### Introduction

As one of the dental specialities, implantology has a long history of innovation and adaptability. Over its long history, it has proven to be a remarkable and innovative branch as it has evolved and responded to the expanding and ever more sophisticated patient needs and new technologies. For decades complete dentures, fixed partial dentures and removable partial dentures were the only treatment modalities available for treating partial or complete edentulism. More than 40 years ago, the advent of endosseous dental implants created a paradigm shift regarding tooth replacement options for patients and it is now considered a well-established treatment modality for partial or complete edentulism.<sup>1</sup>

Implant dentistry has grown leaps and bounds over decades and currently it is at an unprecedented peak. Especially this decade has witnessed huge leaps forward in techniques,

technologies, materials, concepts and philosophies of implant treatment. The entire scope of treatment has progressed originally from tooth replacement to surgically oriented implant reconstruction to the current and more correct prosthetically driven approach to the sophisticated arena of rehabilitation of the stomatognathic system.<sup>2 3</sup>

In less than just a few decades, dental implants have moved from the fringes of dentistry to the mainstream. Indeed, implants are now utilized in situations not foreseen even a decade ago. We need to reflect on the many significant developments in dental implants technology to offer better and a more satisfying treatment option to our patients. This article details the merits of current technologies as well as throws light onto the future of this speciality.<sup>4</sup>

#### A peek into the latest trends

#### **Immediate Implantation with Immediate Temporization**

The original Brånemark protocol published in 1977 influenced implant surgical technique and timing for years. It required that implants be submerged under the soft tissue for at least 4 months and discouraged load during the healing period. As more research accumulated, so did the evidence for unsubmerged implantation (i.e., placement of a transmucosal healing abutment). Barring the need for grafting, one-stage fixture placement is not only acceptable clinically but also easily accepted by patients, as it prevents the need for an uncovering surgery. This decreases the surgical experiences for the patient and minimizes chair time. Another time-saving surgical change is immediate temporization and immediate loading of dental implants within 48 hours of surgical implant placement.<sup>5,6</sup> Case selection can be a thorny issue for these cases. Typically, immediate loading is non-occlusal, that is, non-functional temporization. The interim restoration placed should not occlude with the existing dentition.

It must be noted that hours of judicious multidisciplinary diagnosis, planning, discussion, and laboratory work prior to the surgical appointment are needed, regardless of the corporate protocol used. In the end, case selection becomes the limiting factor. The patient requires a favorable occlusal scheme, sufficient bone to ensure primary stability, good health and a lack of parafunctional habits, among other traits.<sup>7</sup> There is a trend in the direction of this treatment. While early results are promising, this protocol is currently accepted as the standard of care.

#### **Current Augmentation Methods**

The most critical advancement for implant dentistry concerned a philosophical reversal. All too often, restorative dentists were left frustrated by non-favorably placed implants. "Well, that

is where the bone was," was a frequent refrain. Surgeons based implant positioning on the location or availability of the bone, for osseous grafting techniques were in their infancy. Today, this is not the case. The high predictability of current augmentation methods (i.e., block grafting, guided bone regeneration (GBR), sinus elevation) allows for implantation based on prosthetic desires instead of biologic limitations. Thus the treatment goal targets the ideal reconstruction of the dentition. For the vast majority of cases, no compromises founded on anatomy need be made. Significant amounts of horizontal and vertical bony dimension is able to be achieved with GBR. GBR has been shown to equal intraoral onlay grafting with respect to the amount of bone regenerated. Additionally, investigations do not demonstrate resorption of or lower implant survival in regenerated bone over time, when comparing GBR to onlay grafting. Block grafts are not by and large superior to GBR; the evidence simply fails to support that statement.<sup>8</sup>

#### Abutments

Abutment fabrication has and continues to undergo significant metamorphosis. Many abutment options exist: standard machined titanium, standard machined gold, standard ceramic, custom made gold abutments (eg, UCLA) and computer-aided design/computer-aided manufacturing (CAD/CAM) titanium abutments.<sup>9</sup> From a practical stance, implant success criteria include not only stability and function but also esthetic harmony. Depending on the tissue thickness, implant location, and bone level, a standard titanium abutment may appear gray through the mucosa. One solution involves use of abutments constructed from gold or ceramic. In certain cases, the soft tissue will appear healthier and more esthetic. Improved appearance in the presence of a thin mucosa is the goal.

If the implant angulation falls short of ideal, a prefabricated straight or angled abutment may not compensate for off-axis orientation.<sup>10</sup> Custom-made abutments, whether processed by the clinician or industrially, ease the restorative procedure and perfect results. Technology exists that reduces clinical work but still generates an abutment tailored to the individual.

#### **Zirconia Implants**

In recent years, high strength zirconia ceramics have become attractive as a new material for dental implants. They are considered to be inert in the body and exhibit minimal ion release compared with metallic implants. Yttrium-stabilized tetragonal zirconia polycrystals appear to offer advantages over aluminum oxide for dental implants because of their higher fracture resilience and higher flexural strength. Zirconia seems to be a suitable dental implant material

because of its tooth like color, mechanical properties, and therefore biocompatibility. Apical bone loss and gingival recession associated with implants often uncover portions of the metal implant, revealing a bluish discoloration of the overlying gingiva. The use of zirconia implants avoids this complication and accedes to the request of many patients for metal-free implants. The material also provides high strength, fracture toughness, and biocompatibility.<sup>11</sup> The inflammatory response and bone resorption induced by ceramic particles are less than those induced by titanium particles, suggesting the biocompatibility.<sup>12</sup> Although zirconia may be used as an implant material by itself, zirconia particles are also used as a coating material of titanium dental implants. A sandblasting process with round zirconia particles may be an alternative surface treatment to enhance the osseointegration of titanium implants.<sup>13</sup>



**Zirconia Implants** 

Peek (Polyether Ether Ketone) Implants



Following confirmation of its biocompatibility two decades ago, PEEK was increasingly employed as biomaterial for orthopedic, trauma and spinal implants. PEEK is a relatively new family of high temperature thermoplastic polymers, consisting of an aromatic backbone molecular chain, interconnected by ketone and ether functional groups. The chemical structure of polyaromatic ketones confers stability at high temperatures (exceeding 300°C), resistance to chemical and radiation damage, compatibility with many reinforcing agents (such as glass and carbon fibers) and greater strength (on a per mass basis) than many metalsBy the late 1990s, PEEK had emerged as the leading high-performance thermoplastic candidate for replacing metal implant components, especially in orthopedics and trauma. In 1992, PEEK was used for dental applications, first in the form of esthetic abutments and later as implants. Since then many variations in the composition have been carried out to modify and improve upon the working characteristics of the implant. The implants used in had a combination of a phase specific tricalcium-phosphate and titanium dioxide contained within a PEEK matrix. While 80% of the composite was made of PEEK, 20% constituted of beta tricalcium phosphate and titanium oxide combined.

The isoelasticity of PEEK composites ensures that they warp identically to bone and thus produce a more homogenous distribution of stress along the implant bone interface.



**Peek Implant** 

#### **Titanium Zirconium Alloys**

The need for increased mechanical strength from biomaterial implants, both in dental and orthopedic applications, has motivated the search for Ti-alloy alternatives that are free of toxic elements such as vanadium. In dentistry, the use of small diameter implants would be advantageous in situations where single teeth are being replaced or when implants need to be placed within narrow edentulous ridges. However, their use has so far been limited to the "esthetic zone", due to risk of fatigue fracture under high loading. A higher mechanical strength Ti-alloy for small diameter implants would obviate the need for reconstructive surgery and/or

bone grafting or augmentation in the narrow ridges. The titanium-zirconium (TiZr) alloys present as a promising candidate for such applications. <sup>14</sup>

#### PLATFORM SWITCHING

The interface between the abutment and implant, or the microgap, is subject to micromovement and bacterial seeding, and if it lies at or below the crest of the bone, prompts osseous resorption for those reasons. An alternate design for the two-stage implant is platform switching, which is achieved by aligning a relatively wide implant platform to a comparatively narrow abutment and medializes the microgap, thus removing the interface from direct contact with the bone. With possible movement and infection compartmentalized more or less to only the soft tissue, less crestal resorption results. Clinical studies that employ this implant–abutment configuration observe reduced vertical bone loss, even after function. Although a concept that garnered investigation only recently, platform switching data accumulates and shows potential.<sup>15</sup>

### MINI DENTAL IMPLANTS (Mdis)

Every dentist has experienced the problem of dealing with patients with atrophic ridges. The patients always return with complaints of instability of dentures. This problem is more pronounced in the mandibular arch. Traditional dental implants require a period of healing and tissue integration in a nonloaded capacity for optimum predictability. The mini dental implant system (MDIs) can be immediately loaded and provides ongoing stabilization. The advantage in use of MDIs is the minimally invasive, single stage placement procedure, which consists of turning the implant into the bone through a starting opening, but not a prepared bone site. Hence, there is no bone damage or bone wound during implantation. Bleeding and postoperative discomfort are reduced, and most importantly, healing time is shortened.

MDIs are ultra-small diameter (1.8 mm width), biocompatible titanium implant screws, conceived and designed over 20 years ago by a board-certified Manhattan dentist, Victor I. Sendax.

Taking into consideration all advantages of MDI (success rates, surgical technique, financial advantages, possibilities of immediate loading), it can be concluded that MDI are highly successful implant option for edentulous mandible. This fact should be taken into consideration

during prosthetic treatment planning, especially in narrow alveolar ridges and patients who are not able to withstand the costs of more expensive conventional implants of larger diameter.<sup>16</sup>



Mini implant (left) next to a traditional implant.

# **CAD/CAM In Implant Dentistry**

CAD/CAM technology takes implant planning a step further, and enables fabrication of a surgical guide. The surgical guide directs the surgeon in the exact location and angulation to place the implant. There is a growing number of software programs that allow viewing and analysis of the 3D images and subsequent fabrication of a surgical guide. In the youth of implant dentistry, the treatment was surgically driven, meaning that the implant was placed according to the bone available at the time of surgery. This approach eventually proved erroneous, because many implants were placed in locations and angulations that made them difficult or impossible to restore. The evolution has led to a restoratively-driven approach, where the restorative dentist communicates the desired position and angulation via a surgical guide.

The future of dentistry is quickly approaching. Digital impression systems and CAMed models for tooth born restorations are rapidly expanding in the market. Virtual tooth libraries allow CAD/CAM of both provisional and final tooth-born restorations. Numerous implant companies have already designed abutments for compatibility with digital impression systems. Just on the horizon is virtual articulation and virtual tooth arrangement, thus completing the virtual realm of dental technology. It is clear that CAD/CAM technology has transformed all aspects of dentistry, including implant dentistry.<sup>17</sup>



CAD/CAM fabricated surgical guide



Tooth supported CAD/CAM fabricated surgical guide

# **Bioadaptable Dental Implants**

The concept of bio-adaptable dental implants was initially introduced as a customized root mimicking dental implant. By taking advantage of modern computed tomography (CT) techniques and the subsequent analysis capabilities of the scan data and the generation of three-dimensional computer models, in addition to additive manufacturing (AM) and its ability of producing application-specific parts, a cost and time effective track of designing and producing customized dental implants was devised.

The development of specialized software to generate bio-adaptable dental implant designs complying with patients' specifics can drastically reduce the already short lead time. From a clinical concept point of view, the insertion protocol of a bio-adaptable dental implant provides several advantages when compared to the traditional approach. The implantation is executed

in one dental visit in contrast to the three visit protocol discussed earlier. The bio-adaptable implant is customized according to every patient and clinical situation; resultantly it provides optimal function and superior esthetics when compared to stock manufactured implants. In the case where CT scan banks are available, the implant can be ready upon the initial dental visit of the patient where the dentist can atraumatically remove the damaged tooth and insert the implant with minimal to no site preparation. Minimizing trauma will provide with faster healing of the surrounding bone. In addition, the immediate placement can provide immediate esthetics and function.<sup>18</sup>



Design and production of a bio-adaptable dental implants.<sup>18</sup>



# **Center for Dental Implants**

Clinical concept of a bio-adaptable dental implant as a root-mimicking concept.<sup>18</sup>

Socket after

extraction

Extraction of decayed

tooth

Gum 🗧

Jawbone

Insertion of Implant



Geometry of a patient's partial jaw extracted by means of CT analysis.<sup>18</sup>



Two bio-adaptable dental implants with porous rootform built by EBM. <sup>18</sup>

Potential advantages provided by the new concept include:

- $\hfill\square$  Immediate restoration of function and esthetics
- $\Box$  Reduced treatment time
- $\Box$  No to minimally invasive site preparation
- □ Better bite feel due to micromotion capabilities
- $\Box$  Enhanced bone response
- □ Improved patient satisfaction, and quality of life

#### $\Box$ Reduced health care cost

This concept is a new direction in implantology, where the implant matches the patient, instead of the contrary.

#### Surgical Simulation/Surgical Navigation Technologies

To facilitate safe and precise position of implants and avoid potential damage to the vital structures like the mandibular nerve and maxillary sinus two types of computer assisted surgeries are currently available.

As dental implants have become an established treatment, their application to aggressive cases with insufficient quantity and quality of bone has increased. To perform safe and precise surgery, overcoming these difficulties, computer-assisted systems have been developed. There are two major classes of these systems, that is, a computer-guided (static) system and a computer-navigated(dynamic) system.

**Computer guided or computer aided system** –It is a surgical template based system which will optimally determine the position, direction, angulation, diameter and depth of implants.

**Computer navigated system**-It is an advanced form of computer assisted system with implant navigation. The technology offers high motion tracking technologies.

#### Augmented Reality with Surgical Navigation: Future Of Implant Dentistry

Augmented reality is defined as live direct or indirect view of the real physical world whose objects are modified, augmented or supplemented by computer generated sensory inputs such as graphics, sounds, videos etc. In other words, it enhances the person's current perception of reality by superimposing the virtual information onto the real time field.

Unlike an open chest surgery and an open abdominal surgery, looking away from the oral cavity intra-operatively involve a risk of operation errors in case of a dental implant surgery. However, with conventional systems, surgeons have to manipulate instruments in the patient's oral cavity while watching a surgical monitor and they feel anxious during operations. To overcome this problem, a novel surgical navigation system by combining the retinal imaging display (RID) or head mounted display (HMD)and the augmented reality (AR) techniques was developed.<sup>19,20,21</sup>



Schematic illustrations of a surgical navigation system for dental implantology. (a)Conventional approach: A direction of eyes of a dentist is directed to a navigation monitor.(b) Advanced approach: The direction of eyes of the dentist is directed to an oral cavity of apatient.<sup>19,20,21</sup>

#### **Developments In Implant Imaging**

Imaging has always been an important part of dental implant procedures from its beginning. More recently, in the last five years, a revolution is occurring with the availability of "cone beam" CT machines in dental offices and directly in dental surgery enables dentists to manage all the stages, from diagnosis, choice of imaging technique, generation and distribution of imaging data, implant planning, to surgical step. Nowadays radiologist takes place as a specialist in dental imaging, that pays attention to evolution of dental implant techniques.

#### Denta-scanner

It is a very accurate method of jawbone's exploration. It enables dentists to obtain morphological analysis of implant site and bone structure. The initial acquisition gives millimetric slices in axial plan with high resolution. They give different measurements as bone cortical thickness, and dental space.

#### Cone beam CT

It consists of a new device family using cone-shaped X-ray emission. It enables multiplanar reconstructions of dento-maxillary sphere.

The two principal softwares created for dental implant planification are called **Simplant and Nobelguide**, they are mainly designed for surgical act, and a work tool to show dental surgeon the way in implant installation called **Robodent**.

These technologies represent a real and very interesting progress.

As a conclusion, we can see that dental imaging has a major role in implant techniques, with noticeable precision and reliability in pre-implantal planification and surgical help.<sup>22</sup>

IMAGING GOAL	TWO-DI	THREE-DIMENSIONAL IMAGING SOURCES				
	Cephalographic	Periapical	Panoramic	Tomography	Computed Tomography	Cone-Beam Computed Tomography
Bone Height	1	3	2	3	4	4
Bone Width	0	0	0	3	4	4
Long Axis or Ridge	0	0	0	3	4	4
Anatomy Localized	1	1	1	3	4	4
Bone Quality	0	2	2	2	4	3
Pathosis Identified	1	2	3	2	3	4
Jaw Boundaries Determination	1	0	2	3	4	4
Virtual Planning	0	0	1	1	4	4
Guide Fabrication Facilitated	0	0	0	0	4	4
<b>Communication Aid</b>	2	1	2	2	4	4
Benefit/Risk/Cost Ratio	1	1	2	2	3	4

# Value comparison of implant imaging modalities\* commonly used to evaluate implant sites.<sup> $\dagger$ </sup>

\* The imaging modalities are ranked by their ability to satisfy implant planning imaging goals. Ranking scale: 0 = no value, 1 = low value,

2 =mild value, 3 =moderate value, 4 =high value.

<sup>†</sup> Adapted with permission of Journal of the California Dental Association from Hatcher and colleagues.<sup>1</sup>

# **Application of Lasers in Dental Implants**

The parallels in the expansion of implant dentistry and laser dentistry in clinical practice are apparent. As advocates for laser dentistry continue to seek new ways to use the technology and as more practitioners become involved in implant dentistry, it is logical to see the concurrent use of both technologies in clinical practice.<sup>23</sup> Commonly used lasers in implantology include: Diode, Er:YAG, Er,Cr:YSGG, Nd:YAG, CO2

# **APPLICATIONS**

- Second-stage surgery of submerged implants
- Removal of peri-implant hyperplastic overgrowths
- Treatment of peri implant lesions
- Decontamination
- Surface characterization of implants
- Sinus lift procedures
- Block grafting
- Implant placement

# ADVANTAGES

- Dry and bloodless surgery
- Instant sterilization of the site
- Reduced bacteremia.
- Reduced mechanical trauma.
- Minimal post-operative swelling and scarring
- Minimal post-operative pain
- Lasers can achieve excellent tissue ablation with bactericidal and detoxification effects
- Less wound contraction
- Prevents the production of matrix-metalloproteanases (collagenase, gelastase, elastase, protease) which break down soft tissue, cause edema/erythema, and have an osteopromotive effect on osteoclasts.<sup>23</sup>

# Stem Cells in Implant Dentistry

The recent increase in the demand for dental implants has generated a need for robust bone augmentation in the atrophic alveolar ridge and the maxillary sinus. The Academy of Osseointegration stated in its 2010 Silver Anniversary Summit that the continued improvement of the dental implant success rate will require stem cell-based technologies, as osteogenic stem cells in an implant osteotomy site could provide the necessary factors to form superior bone that could contribute to enhanced long-term success of the implant treatment. Such an approach would decrease the need for a GTR membrane and could be used as a single product without requiring other adjuncts. Stem cell therapy is also potentially important for patients with compromised vascular supply and impaired wound healing because it may be able to improve vascularity to facilitate hard tissue augmentation at local sites. Therefore, stem cells seem to present a promising strategy to achieve the regeneration of large alveolar bone defects, particularly to provide stable and accelerated bone formation as well as enhanced osseointegration in dental implant treatments.<sup>24, 25</sup>

#### Conclusion

Implant dentistry is also progressing rapidly today largely due to technological innovations. As we look ahead the future will definitely bring about more advances as our technological skills, research efforts and abilities improve. There are numerous areas for future developments in dental implants, hence it is reasonable to look forward to the further transformation of this industry from a complex, esthetic, surgical and functional dilemmas into simpler rehabilitation solutions.

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#### **Original research**

#### Dynamic Visual Acuity Between Frisbee Players and Non-Frisbee Players

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#### Abstract

**Background:** Dynamic visual acuity (DVA) is the ability to resolve a moving stimulus. Dynamic visual acuity is in general superior in athletes than non-athletes, which contribute to better visual abilities and translate to better performance. In this study, it is hypothesized that Frisbee players have better dynamic visual acuity due to greater perception of active images through perceptual learning from the constant tracking of Frisbee discs at a vertical and horizontal trajectory.

**Materials and Methods**: To measure dynamic visual acuity, participants were asked to indicate the orientation of a broken ring like a Landolt C while it traverses across a screen in the two trajectories with a computerized software (DinVA 3.0 software<sup>8</sup>).

**Result:** Frisbee players (n=17) showed no significant difference in mean DVA at both the meridians (V:0.377m/s+0.05; H:0.394m/s+0.05) compared to non-Frisbee players (n=33) (V:0.396m/s+0.09; H:0.405+0.08). Similarly, within group analysis showed non-Frisbee players had no significant difference (p=0.327) between vertical and horizontal DVA. However, there was a statistical significance (p=0.017) between the vertical and horizontal mean DVA in Frisbee players.

**Conclusion:** This concluded that there was no significant difference between the two groups but may suggest that Frisbee training does improve dynamic visual acuity but in the horizontal meridian due to a constant and improved tracking ability to predict horizontal stimulus.

Keywords: Dynamic Visual Acuity, Frisbee players, Static visual acuity, Landolt C

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#### Introduction

Vision provides functional information to conduct actions and motor behavior of a living being to react to its environment. Dynamic visual acuity (DVA) is briefly described as the ability to resolve a relatively moving stimulus<sup>1</sup>. They are part and parcel of our daily lives and seemingly essential for activities that require stimulation of precise and clear vision whilst in moving or dynamic environments. These activities include video games, driving, piloting, sports and scrolling on screens. Thus, suggesting that DVA is a more practical estimation of visual performance for everyday conditions rather than static visual acuity<sup>2</sup>. However, while static visual acuity (SVA) only targets to resolve a stationary stimulus, it is also one of the rudimentary visual functions and is involved in various other important visual functions.

These oculomotor abilities and system, consisting of rapid eye movements such as saccadic and pursuit movements<sup>1</sup> with saccadic eye movements thought to be a pivotal role in tracking moving targets at high speeds<sup>3</sup> while pursuit eye movements being a visual analysis of moving objects by stabilizing the retinal image on the fovea. With sports known to enhance the visual prowess of an individual, it was reported that athletes resulted in better DVA<sup>4.</sup> Hence, the interest came about to identify if DVA can be improved by the regular practice of the sport ultimate Frisbee. Hypothesizing that the ongoing practice of the athlete to respond to the constant rapid eye movements towards the flying disc in their frontal and peripheral vision allowed merits to sustain its visual ability.

DVA is relatively important in sports, especially when involving high speed movements. Such studies have reported increased DVA in athletes with correlation to the ability to track moving targets<sup>5</sup>. These sports that showed increased DVA in athletes include water polo<sup>6</sup>, baseball<sup>5</sup>, tennis and badminton<sup>4</sup> and softball<sup>7</sup>. Sports in general are known to have a certain effect on a person's visual ability and prevent the attenuation of cognitive processing speed as they age. Hence, the interest came about to identify if participating in playing the sport, ultimate Frisbee, has made any inclination towards that direction. In addition, there are a variety of research done in comparison of the effect of different sports on DVA of participants and non-participants of the sport. However, little is known about the effect and difference of DVA trajectory.

Therefore, a specific and fixed direction from a vertical and horizontal trajectory was chosen to identify whether there are any differences in participants of the sports Frisbee and nonparticipants. The aim of this study is to examine the effect of dynamic visual acuity on Frisbee players by measuring their performance against the performance of sedentary individuals control group at different eye movements, specifically vertical and horizontal movements.

#### Methodology

The measurement for DVA was performed using a 17.5inch Pavilion HP laptop with a desktop resolution of 1366 x 768, refresh rate of 60Hz in an 8-bit depth and a Standard Dynamic range (SDR) of colour space. The software (DinVA 3.0 software<sup>8</sup>) was projecting a moving Palomar Universal Optotype stimulus across the screen horizontally, vertically, and diagonally.

The subjects were students and lecturers from SEGi University as well as frisbee players from Carebears Ultimate Frisbee Club (CUFC). Consent form and a questionnaire was given to patients to fill to see if they are eligible to be an ultimate Frisbee player or a non-Frisbee player which is subjected by the inclusive and exclusive criteria. The experiment was done in a dimly lit room to be isolated from anyone else but only examiner and subject. The room lux is around 100-200 cd/m<sup>2</sup> and the screen lux to be around 60-80cd/m<sup>2</sup>. The subjects were to be seated at 2 meters from the monitor with the viewing distance to be monitored constantly throughout.

At first, the static visual acuity (SVA) was to be taken to ensure visual acuity of 6/9 or better before proceeding. It was done with a computerized SVA software. The size of the letter optotypes are set to be compensated to the distance of 2 meters. The subjects are to read the letter optotypes on the screen and until he or she incorrectly identifies at least 4 letters in the line. The SVA results were recorded in LogMAR. An addition of a contrast sensitivity test and a developmental eye movement test was done to see if there were any significant binocular vision abnormalities.

During DVA testing, the subjects were given a practice trial of each direction once to familiarize with the structure of the software and the keyboard keys. The test was started with high speed (0.881 m/s) with the horizontal direction and pressing the "S" button will signal the start of the test. There will be a moving Palomar Universal Optotype which the ring gap will appear facing any direction at random, pressing the appropriate directional key will signal the next moving target. Each test was done with a trail of 3 times and the mean DVA results were recorded. After that, the setting was changed to the vertical direction with the same sequence.

The Shapiro-Wilk test with independent T test and paired-t test was used for the analysis using IBM SPSS software (version 25, SPSS Inc.)

# Results

A total of fifty-five subjects participated in this research. The mean age for Frisbee players were  $25.64 \pm 7.5$  years and the non-Frisbee players were  $23.24 \pm 5.5$  years. There were 10 males (58.82%) and 7 females (41.18%) Frisbee players while the non-Frisbee players had 9 males (27.27%) and 24 females (72.72%). Data on the DVA were all normal hence a parametric test was used to further analyze the data.

The mean values of DVA for the Frisbee players and non-Frisbee players are shown in table 1. The mean difference showed that the overall DVA Horizontal was higher than the overall DVA Vertical score, while the overall DVA score of non-Frisbee players was higher than the Frisbee players.

There was a statistically significant difference between DVA Horizontal ( $0.398 \pm 0.0509$  m/s.) and DVA Vertical ( $0.337 \pm 0.0545$  m/s) among the Frisbee players, a higher score on the DVA Horizontal, t (15) =2.686, p<0.05. However, similar pattern was observed among the non-Frisbee players but statistically there was no significant difference. Comparison of DVA vertical and horizontal among both the groups show no statistical significant difference.

	Group	Ν	Mean	Std. Deviation	p value
Frisbee	DVA_V	17	0.337	0.0545	<0.05*
	DVA_H	17	0.398	0.0509	_
Non-Frisbee	DVA_V	33	0.396	0.0912	0.327
	DVA_H	33	0.405	0.0773	_
DVA_V	Non-Frisbee players	33	0.396	0.0912	0.365
	Frisbee players	17	0.377	0.0528	_
DVA_H	Non-Frisbee players	33	0.405	0.0773	0.546
	Frisbee players	17	0.394	0.0517	_

Table 1 Mean, standard deviation, and p value of the Dynamic Visual Acuity scores of the non-Frisbee players and Frisbee players

\* Significant distribution

#### Discussion

The main aim for this study was to investigate the possible changes in DVA of players and non-players in the specific sport Frisbee, and whether with different directions had any part to play on DVA. In which the vertical meridian being bottom-up movement and horizontal movement being right-to-left movement. First, it was observed that there were no significant differences in the results of DVA exhibited between the Frisbee and non-Frisbee players, but non-Frisbee players scored overall higher than the Frisbee players. Secondly, the Frisbee players exhibited superior horizontal mean DVA compared to their vertical mean DVA. Finally, the horizontal DVA was overall higher than the vertical DVA in both groups of the Frisbee and non-Frisbee players with no clinical significance.

There are a variety of research that compared the visual abilities showing athletes had a likened superiority compared to the non-athletes but showed no differences between non-athletes and beginners of their sport. This was observed by studying the comparison of facility of accommodation and saccadic eye movement (SEM) differences in volleyball players and non-players<sup>9</sup>. They took three groups of people consisting of a first group of 22 advanced national players with 12h/week with at least 5 years of experience, a second group of 21 intermediate players with 7h/week and the third group of 22 non-serious players who played leisurely with no training programme. A group of 20 non-players was assigned as the control group. They found that the visual abilities were significantly (p<0.001) better for the advance players compared to the beginner players and non-players while the intermittent players did not show any significant differences from the advanced players, same results go when comparing the beginner players to the non-players.

This could explain the unobserved clinical significance between Frisbee players and non-Frisbee players in the present study as the Frisbee players that participated in the study were fanatics of the sport and were not under any national or training programme. This could be compared to the beginner players and non-players comparison of the cited study that had no significant differences as they only participated at a level of leisure. The visual prowess of the Frisbee players did not receive the potential development to show any differences even though the participants of the present study had an experience of at least two years and had been having 6h/week of playing Frisbee.

Furthermore, research suggested that players who participate in other fast ball sports such as softball<sup>7</sup> showed higher mean DVA skills where the players were focused on following the ball

pitched at a high speed. Similar to volleyball<sup>9</sup>, with the players constantly tracking the ball to predict the spatial location and speed that is travelling to make good judgements and outcome due to the nature of the sport. Whereas Frisbee players are occupied by looking at players more rather than the Frisbee disc flying as it is a team sport with the nature of the game like American football. This is especially evident when players are playing "defense" with all their focus appointed to the other players to track their movements rather than the Frisbee disc.

The difference in visual skill between professional rugby and non-professional rugby players hypothesized on an athlete's ability to excel at their sport due to their superior visual abilities or through the continuous training that to develop the necessary skills that aided in performance<sup>10</sup>. It was concluded that it was through the contribution of the vigorous and constant practice to train their skills that enabled them to excel, and superior visual abilities may be insignificant.

Other studies further provided evidence of unobserved differences of mean DVA between athletes and non-athletes, similar to current study. There were 30 elite national water polo players, 13 sub-elite players and 30 sedentary students<sup>6</sup>. They used the computer soft software (DinVA 3.0)<sup>8</sup> which was made for DVA testing with different directional trajectories. They concluded that the sedentary students, sub-elite, and elite players showed no clinical significance of mean DVA scores between the three groups but revealed that a significant interaction of certain conditions of speed, contrast, and trajectory in which sub-elite and elite performed better than the sedentary students.

In the present study there were no significant interaction between the Frisbee and non-Frisbee group, however there was a significant difference between directions of DVA, the mean of horizontal DVA being superior to the mean of vertical DVA of Frisbee players. This occurrence can be assumed as the movement of a Frisbee disc, is mostly horizontal, being swung around from one point to another by the players and done consciously and purposefully. As there is a lack of study done on the effects of ocular-exercise on athletes, The effect of oculomotor exercises on DVA and the limit of stability in female basketball players was previously studied<sup>11</sup>. This study had thirty female athletes with a minimum of three years of basketball activity and where they had the intervention group to perform exercises while sitting for four weeks, 10 minutes each time in the morning and evening. This exercise can be explained as saccadic and pursuit trainings done with the change of gazes or head movements with a ball in hand while sitting down, with it done all in the horizontal trajectory. They concluded that there

was a significant difference (p<0.001) in mean DVA and overall stability index in the intervention group after doing the exercise.

As a result of constant and fast horizontal head movements and saccadic gazes practiced by Frisbee players in training to successfully resolve their desired target whilst in game, it may contribute to the explanation of the observed significance. Furthermore, a similar study on the effectiveness of oculo-motor exercises and gaze stability exercises on postural stability and DVA in healthy young adults where the 28 intervention groups did gaze stability exercise for three weeks<sup>12</sup>. The before and after postural stability by standing quietly, standing with active rotation, and DVA were measure. They found that there were significant differences in the standing with active head rotation and the DVA in the intervention group. They theorized that the improvements of results were due to the improved neural adaptation of the vestibular nuclear complex, increased vestibule-spinal function and enhanced central pre-programming. This can further clarify on the speculation that the function of 'exercised' horizontal head movements can result in the brain to produce predictive programming to adapt.

The idea that constant external stimuli can develop improvements in the visual system is observed in the present study, which overall horizontal DVA is higher than the vertical DVA in both Frisbee and non-Frisbee players. One could hypothesize that it can be due to the nature of our environment and daily activities. Relating to peripheral visual cues and the tracking of the eye to objects in our environment such as moving transportation vehicle and reading which are mostly horizontal movements which can assume it to be the most frequently used amongst the other movements such as vertical and oblique movements.

This hypothesis can be further be made more concrete through the anatomical orientation in the brain where horizontal or vertical stimuli are better resolved rather than oblique, coining the term the "oblique effect". This effect is further studied by and states that both widths and numbers of cells of their orientation tuning differs as function of preferred orientation<sup>13</sup>. In which cells tend to be orientated in horizontal and vertical rather than oblique angles and that most cells that are triggered are horizontal orientations. Their study observed that horizontally tuned cells have a better non-linear component than those tuned to other orientations. This can be translated into the preference of better resolve of horizontal stimuli.

In summary, the results of the present study are in contrary with the previous studies of DVA being superior to those who participate in sport5<sup>5,6,7</sup>, but does improve with constant activation through specific exercises. A possible limitation in the present study is the limited amount of

training and experience in the Frisbee players that participated and that the characteristic of the DinVA test were not sensitive enough to detect any distinction to be noticed due to the nature of the test being a software configuration rather than a hardware configuration.

# Conclusion

This study showed Frisbee training does improve DVA in the horizontal meridian. However, there are no differences in DVA between Frisbee players and non-Frisbee players.

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### **Case report**

# Measuring Scleral Lens Vault with Accuracy – A Case Report

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#### Abstract:

Keratoconus is a non-inflammatory ocular pathology affecting the cornea's shape due to thinning and protrusion. This condition can be unilateral or bilateral with asymmetric presentation between both eyes. Refractive correction with spectacles is helpful in the initial stages; however, contact lenses play a significant role in the advance stages. Various options for contact lenses are available, and practitioners can use those depending upon the severity of the condition, shape of the cone, and other factors. Scleral lenses have gained popularity in recent years because they vault over the cornea and the limbus with no touch and land on the sclera. Caution is warranted on the amount of vault created between the scleral lens and the cornea; hence accurate measurement can be a valuable tool for practitioners' confidence in prescribing these lenses. This case presentation summarizes the use of Anterior Segment Optical Coherence Tomography (AS-OCT) to accurately measure the vault and finalize the lens fitting.

Key Words: AS-OCT, corneal topography, cross-linking, Keratoconus, scleral lenses

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#### Introduction:

Keratoconus is a non-inflammatory ecstatic disorder of the cornea causing corneal protrusion and thinning, resulting in poor vision because of irregular astigmatism <sup>1</sup>. Due to the anatomical and optical irregularities, it presents challenges to achieve the best visual outcome. Spectacles can be used at the early stage of keratoconus, while due to the higher-order aberrations (HOAs) in advance stages, specialty contact lenses may be required to reduce HOAs by masking the corneal irregularities. With a range of specialty contact lens options now available, including specialty soft, custom-made corneal gas permeable (GP), piggyback, hybrid and scleral lens, clinicians fit patients successfully.<sup>2</sup>

Scleral lenses were initially designed to correct myopia and irregular cornea and one of the most cited contact lens options for keratoconus management <sup>3</sup>. This is because scleral lenses provide stable fitting with improved comfort even in advanced cases of keratoconus. A recent survey shows that the use of scleral lenses has increased <sup>4</sup>. This could be because the lenses also allow individual customization to provide a maximum visual outcome. Incorporating technologies such as the anterior segment optical coherence topography (AS-OCT) helps clinicians to observe the fitting accurately and measure the vault accurately, thereby improving the clinicians' confidence in fitting these lenses <sup>5</sup>.

#### **Case Report**

#### **Initial visit**

A 28-year-old Indian male presented to the contact lens clinic for a new contact lens fitting. He was diagnosed with keratoconus in both eyes and had undergone corneal cross-linking in both eyes eight years ago. He had no family history of keratoconus, and he had no known drug allergies. The patient was a student studying master's in accounting. He had been wearing Rose K lenses (infrequently) since he was diagnosed with the condition. He was unaware of the specific design and parameters of the lenses. He had last worn his lenses a week back. He had been wearing spectacles most of the time. The reason for infrequent contact lens wear was due to the low level of comfort even though the visual quality was good. He had read about scleral lenses online and had come with a particular interest to try scleral lenses for his condition.

On examination, his corrected distance visual acuity with his habitual correction was 6/18, improving to  $6/18^{+2}$  in the OD and 6/12 with no further improvement with a pinhole in the OS. His habitual Rx measured using the focimeter was  $-2.50 - 3.25 \times 45$  OD and  $\pm -2.75 \times 140$  OS.

Extraocular motility was SAFE without pain or double vision. Pupils were equal, round, and reactive to light with no signs of relative afferent pupillary defect. Manifest refraction was  $-2.50 - 3.25 \times 30$  OD and  $\pm -2.75 \times 140$  OS with best-corrected distance visual acuity of 6/12 OD and 6/12 OS. Manifest refraction was noted to have a shift in the cylinder axis by 15 degrees for OD. Slit lamp biomicroscopy revealed the ocular adnexa's normal appearance, lids, lashes, conjunctiva, and cornea on both eyes with no clinical signs of keratoconus seen. No significant corneal staining was detected on staining the eye with 1mg Fluorescein Sodium LP moisten with normal saline. The tear breakup time (TBUT) was 8 sec OD and 9 sec OS. The patient's corneal thickness measured on the 3D OCT-1 Maestro AS-OCT was 442 microns on OD and 479 microns on OS.

The horizontal visible iris diameter (HVID) measured was 11mm on OD and OS, while the pupil size was 4.5mm on OD and OS under normal room illumination.

Corneal topography examination was performed using Tomey TMS-4 Topographic Modelling System (Tomey Co., Ltd., Nagoya, Japan). The results were the baseline topography values shown in Figures 1 and 2. On performing keratoconus screening on Tomey TMS-4, it showed 77.2% severity in OD and 82.9% severity according to Smolek / Klyce Screening. The Amsler's – Krumeich classification for keratoconus can be classified as Stage II for OD and Stage III for OS.

The options for vision correction for this patient based on the condition included:

- Spectacles
- Soft toric lenses / Customized soft toric lenses
- Rose K2 NC lens design
- Scleral lenses





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#### Figure 1

**Figure 1**: Corneal topography measured using Tomey TMS-4 Topographic Modelling System (Tomey Co., Ltd., Nagoya, Japan). Figure 1 shows the right eye's axial map, and Figure 2 shows the left eye's axial map. This shows that the left eye was more affected compared to the right eye.

Since the patient was not comfortable with his own Rose K lenses, it was decided to fit him with Rose K2 XL, the corneo-scleral lens design. Based on the recommended fitting guide, the initial lens parameters were calculated as shown in Table 1

Parameter	OD	OS
Base Curve	6.90 mm	6.70 mm
BVP	-7.00 D	-9.00 D
TD	14.60mm	14.60 mm

**Table 1:** Parameters of the initial trial lens based on fitting guide.

#### Trial #1

The lenses were inserted on both the eyes are the fitting evaluation was performed after 15-20 minutes of adaption time. The lenses were filled with normal saline before insertion. The dynamic fitting assessment a post blink movement of about 1-1.5mm on both eyes. The fluorescein pattern of the right and left eye is shown in Figures 2a and 3a, respectively. Figure 2a shows the right eye lens's fluorescein pattern was too flat as there was a central touch seen just at the cone apex position, while Figure 3a shows the left eye lens's fluorescein pattern flat to the optimum amount of fluorescein.

AS-OCT was performed using the 3D OCT-1 Maestro to measure the tear layer, referred to as vault. This showed that the vault was extremely low for the right eye (46 microns) shown in figure 2b, whereas it was near to adequate for the left eye (179 microns), as shown in figure 3b. There was also a large clearance zone at the lens's edge inferiorly due to excessive edge lift for both eyes.

These findings concluded that the fitting was very flat for the right eye, and it was optimum to flat for the left eye. Hence, both lens base curve was steeped. The parameters of Trial 2 are shown in Table 2.







**Figure 2 and 3**: Fluorescein pattern for the right eye is seen in figure 2a, and corresponding AS-OCT is seen in figure 2b, which shows touch at the cone apex and a low vault, respectively, indicative of a flat fit. Figure 3a shows the left eye's fluorescein pattern with the corresponding AS-OCT seen in Figure 3b showing a feathery touch with near to adequate vault indicative of an optimum to flat fit.

Table 2: Parameters	of the	lens for	Trial 2	

Parameter	OD	OS
Base Curve	6.60 mm	6.60 mm
BVP	-10.00 D	-10.00 D
TD	14.60mm	14.60 mm

# Trial # 2

Based on the parameters in Table 2, lenses were inserted in both eyes, and fitting was assessed after 15-20 minutes of lens insertion. The dynamic fitting assessment a post blink movement of about 0.50 to 1mm on both eyes. The fluorescein pattern of the right and left eye is shown in Figures 4a and 5a, respectively showing an acceptable fluorescein pattern for both eyes.

AS-OCT was performed using the 3D OCT-1 Maestro to measure the tear layer, referred to as vault. This showed that the vault was acceptable for both eyes with these lenses. The vault was for the right eye was 258 microns (Figure 4b), and the left eye was 247 microns (Figure 5b). The edge lift was asymmetric between the vertical and horizontal meridian, specifically in OD; however, no modifications were made to the edge profile for both the eyes.

















Figure 4 and 5: Fluorescein pattern for the right eye is seen in figure 7a, and corresponding AS-OCT is seen in figure 7b, which shows acceptable fitting with adequate vault, respectively. Figure 8a shows the left eye's fluorescein pattern with the corresponding AS-OCT seen in figure 8b, which also shows acceptable fitting with an adequate vault. Both eye fitting is accepted.

These findings obtained with trial 2 indicated that the fitting was acceptable. Over-refraction was then performed on both eyes, which showed  $+0.50 - 1.75 \times 145$  OD and  $+0.50 - 1.50 \times 140$ OS with vision improving to 6/6 on both eyes monocularly. The parameters of the final lens ordered for the patient are shown in Table 3.

Parameter	OD	OS
Material	Boston XO2	
Base Curve	6.60 mm	6.60 mm
BVP	-9.50 / -1.75 x 145	-9.50 / -1.50 x 140
TD	14.60mm	14.60 mm
Edge profile	Standard	Standard

**Table 3:** Final lens parameters ordered for the patient.

# Lens Dispensing Visit

The patient came to the clinic for his lens collection. The patient was taught lens insertion, removal, lens handling. The fitting assessment was carried with the lenses, and the fitting obtained was like the fitting which was finalized before lens ordering Distance visual acuity with lenses was  $6/7.5^{+2}$  on OD and 6/7.5 on OS. The patient was comfortable, and the lenses were dispensed. His subsequent follow-up was scheduled a week later.

# Follow Up #1

After about three and a half months, the patient returned to the clinic as he had to travel for his internship. The patient was regularly in touch via WhatsApp and reported that he had no problems in comfort and the vision was good. He was wearing the lenses most of the days for more than twelve hours without any problems.

The patient had worn the lenses for about five hours during this follow-up visit. Distance visual acuity with the lenses was  $6/6^{-3}$  on OD and  $6/7.5^{+2}$  on OD. An over-refraction of +0.50D was found, but it did not change the best-corrected visual acuity at a distance as well as near. The fitting assessment showed adequate lens movement of about 0.5mm to 0.75mm and an acceptable fluorescein pattern on both eyes.

AS-OCT was performed using the 3D OCT-1 Maestro to measure the tear layer, referred to as vault. This showed a decrease in the vault compared to the final lens fitting. The vault was for the right eye was 147 microns (Figure 6), and the left eye was 158 microns (Figure 7).

There were no signs of any corneal staining or conjunctival indentation on ocular examination post lens removal; hence no modifications were made, and the patient was recommended to follow up every three months.









**Figure 6 and 7**: AS-OCT for OD (Figure 6) and OS (Figure 7) performed using the 3D OCT-1 Maestro on follow-up showing reduction of vault compared to the finalized fitting vault.

#### **Discussion:**

The prevalence of keratoconus varies depending upon the geographic location, diagnostic criteria, and the study population.<sup>6</sup> The prevalence in a clinic-based population study showed approximately 1 in 100 patients who visited a cornea specialist center in Malaysia.<sup>7</sup> Keratoconus clinically presents in patients in their teenage years or early twenties. A study reported that most keratoconus patients seen university hospital in Jordan were between the age of 20 to 24 years old (mean age of 25.9 years).<sup>8</sup> Their main complaints are progressive blur vision and distortion secondary to myopia and astigmatism. Glare resulting due to photophobia and monocular diplopia could also be a presenting symptom. Various ocular signs involving a different layer of the cornea can be seen based on the stage of the disease, commonly seen scissors reflex during retinoscopy, Fleischer's ring within the epithelial layer, and Vogt striae within the stroma. Munson's sign, which is the protrusion of the lower lid during down gaze, can be seen in the disease's advanced stage. Hydrops can be seen due to the spontaneous teas in the ruptured Descemet's membrane.

Corneal mapping using a topographer can be a valuable diagnostic tool for detecting subclinical keratoconus and monitoring the disease's progression. A topographic classifier using eight indices to diagnose keratoconus is available.<sup>9</sup> Different topographic devices provide additional information through various features to help clinicians detect keratoconus at an early stage. This will help determine the contact lens design and parameters and help clinicians decide on other strategies such as collagen cross-linking (CXL), intrastromal corneal ring segments, phakic intraocular lenses, and others to slow down the progression of the disease.<sup>10</sup> Keratoconus was classified using the Amsler-Krumeich (AK) system for grading proposed by Mark Amsler in 1947. This was based on keratometry (central anterior corneal curvature) and optical pachymetry (apical thickness). The AK system has limited usefulness due to modern imaging, which allows for detecting the disease at a much earlier stage. Placido -based corneal topography is still widely used; however, there is a drawback as it completely ignores the posterior cornea. The new Berlin ABCD classification system was introduced by the Oculus Pentacam (Oculus GmbH, Wetzlar, Germany) to overcome this shortcoming.<sup>11</sup> The ABCD criteria is also used to monitor the progression of keratoconus, and a study states that corneal cross-linking would effectively stabilize the progression of keratoconus as per the ABCD criteria.<sup>12</sup> Keratoconus can also be classified using a statistical approach into five levels reported to be free from subjective considerations using the Simulated keratometry (SimK), Central K, Cone location and magnitude index (CLMI), Higher-Order root mean square (Ho RMS), logBC, and coma.<sup>13</sup>

A variety of contact lens options are available for patients with keratoconus ranging from soft toric contact lenses to scleral contact lenses. The lens selection depends on various factors such as the corneal topography, previous experience with contact lenses, visual demand requirement, to name a few.<sup>14</sup>

A well-fitted scleral lens must fulfill these three criteria: vaulting over the cornea and limbus, ensuring a proper landing zone over the sclera with adequate tear exchange underneath the lens. This will ensure maintaining good corneal physiology.<sup>15</sup> The Rose K XL lenses were developed by Paul Rose and have been studied in patients with irregular corneas showed that these lenses provided qualitative as well as a quantitative visual function along with high degrees of patient comfort and satisfaction.<sup>16</sup>

The initial lens was selected for this patient based on the manufacturer's Rose K2 XL fitting guideline. After computing the mean K from the topography results, the lenses were selected, which was 6.58mm in OD and 6.05mm in OS. Hence, looking at the practitioner guidelines' initial base curve of the trial lens was 6.90mm for OD and 6.70mm for OD.

Generally, a five-step fitting approach is suggested for a scleral lens, including diameter selection, clearance (vault measurement), landing zone fit, lens edge assessment, and asymmetrical back surface design. Lens vault and landing zone can be clinically observed through the slit lamp – with and without fluorescein. This is done by comparing the slit width of the space between the lens and the cornea (vault) with the known thickness from either the

contact lens thickness or the corneal thickness. However, this is an approximation. It has been reported that an approximate underestimation by 50 microns would be there when measuring vault with slit lamp compared to the ultrasound measurements.<sup>17</sup> AS-OCT is a valuable tool to accurately measure the vault allowing clinical to modify the sagittal height to obtain the required vault.<sup>18,19</sup>

AS-OCT has numerous research and clinical applications for glaucoma<sup>20</sup>, refractive surgeries<sup>21</sup>, corneal transplants<sup>22</sup>, pachymetry<sup>23</sup>, corneal diseases<sup>24</sup>, and many more<sup>25</sup>. The use of AS-OCT has now been expanded for pre-and post-contact lens assessment (especially specialty contact lens fittings and custom designing of large diameter scleral lenses).<sup>26–28</sup> This is because it allows to measure the tear layer (vault) accurately and look at the interaction between the lens edge and the sclera. AS-OCT is, therefore, a useful tool to observe how the parameter change affects the lens fitting, as discussed in this case presentation.

The 3D OCT-1 Maestro is a noncontact SD-OCT. It is a fully automated instrument that captures 50,000 axial scans per second. A study comparing the OCT model across seven centers and the measurements were reliable in normal healthy individuals.<sup>29</sup> It is also understood that the scleral lens, once dispensed, usually continues to settle in the first or second month of lens wear. Appropriate measurements can help measure these changes accurately and be used to assess the vault and clinical performance of the scleral lens over time.<sup>30</sup> A review article published reports that an OCT imagining is the most accurate and repeatable corneal vault estimate.<sup>31</sup>

The central clearance (vault) for the patient was seen to be reduced after about three and a half months of wear in both eyes by nearly 100 microns. A study that compared the change in vault during scleral lens wear with AS-OCT after 1 hour and 4 hours of wear reported a significant reduction in the vault after 4 hours of lens wear with an average reduction of 125 microns in the ectasia group using the PROSE lenses.<sup>32</sup> Another study also reports similar findings with three different lens designs.<sup>33</sup> Both the studies suggested that a sufficient amount of time should be allowed before finalizing the fit (4 hours to 8 hours), and it was also reported that larger diameter lenses had more significant changes than smaller diameter lenses. In clinical practice, one should select the fit with a slighter higher than required vault to the account of the lens settling over time.

A study compared how varying degrees of corneal clearance of scleral contact lenses affect visual acuity and comfort in corneal ectasia patients. The results demonstrated that variation in

the central clearance did affect the vision and comfort. Increased clearance may not provide the best vision.<sup>33</sup> This could be why the vision improved by a couple of letters on the follow-up visit for this patient compared to the dispensing visit.

# Conclusion

In conclusion, AS-OCT would be a valuable tool in lens choice, accurately measuring the vault of the lens over the cornea and monitoring it over time and looking at the landing of the scleral lens edge over the sclera. All these would help clinicians to modify and alter the fitting of the lens as desired with confidence.

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