RETINA PODCAST

Review

SUPRACHOROIDAL SPACE INJECTION TECHNIQUE

Expert Panel Guidance

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Purpose: To develop professional guidelines for best practices for suprachoroidal space (SCS) injection, an innovative technique for retinal therapeutic delivery, based on current published evidence and clinical experience.

Methods: A panel of expert ophthalmologists reviewed current published evidence and clinical experience during a live working group meeting to define points of consensus and key clinical considerations to inform the development of guidelines for in-office SCS injection.

Results: Core consensus guidelines for in-office SCS injection were reached and reported by the expert panel. Current clinical evidence and physician experience supported SCS injection as a safe and effective method for delivering retinal and choroidal therapeutics. The panel established consensus on the rationale for SCS injection, including potential benefits relative to other intraocular delivery methods and current best practices in patient preparation, pre- and peri-injection management, SCS-specific injection techniques, and postinjection management and follow-up.

Conclusion: These expert panel guidelines may support and promote standardization of SCS injection technique, with the goal of optimizing patient safety and outcomes. Some aspects of the procedure may reasonably be modified based on the clinical setting and physician judgment, as well as additional study.

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Intravitreal injection (IVT) injection (Figure 1) is the most common route of delivery of retinal therapeutics, with well-defined procedural guidelines.[1] However, IVT injection can also present challenges that depend in part on the therapeutic agent.[1] For example, IVT delivery might in some cases result in variable or incomplete spread to the deep outer retina or choroid, unwanted diffusion to the anterior segment,[1,2] or temporary disruption of vision due to dispersion of particulate, nontranslucent drug particles—a phenomenon referred to as "snow-globing." Subretinal injection, an alternative to IVT delivery, has also been used for targeted delivery of retinal gene therapy and stem cell–derived retinal pigment epithelium among other therapeutics,[3] but administration requires pars plana vitrectomy and retinotomy, after which delivery is restricted to a limited area at and around the point of delivery.[1,4,5] Variable delivery, for example due to drug reflux through the retinotomy, and postsurgical complications, including retinal detachment and epiretinal membrane proliferation, can present challenges.[2,4,6]

Injection into the suprachoroidal space (SCS) presents an opportunity for targeted delivery of high levels of injectate directly to affected chorioretinal

tissues.[2,4] The SCS is a key site in uveoscleral outflow, situated between the choroid and sclera. This choroid-adjacent potential space expands with the introduction of fluid and serves as a drainage path from the front to the back of the eye, thereby contributing to the normal maintenance of intraocular pressure (IOP).[2,7,8]

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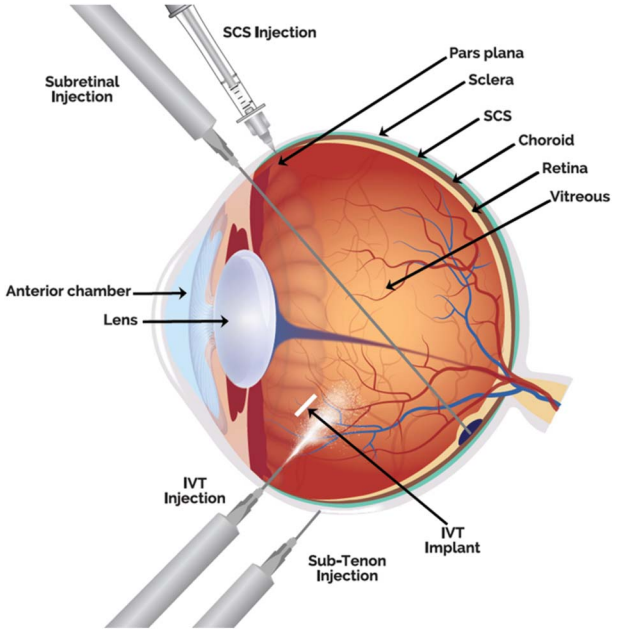

Fig. 1. Diagram of the anatomy of the eye and schematics of subretinal, sub-tenon, IVT, and SCS injection. Adapted from Ciulla et al. *Am J Manag Care* 2022 and reproduced with permission from Clearside Biomedical, Inc.

Approaches to SCS delivery include microcatheterization and microneedle injection. During microcatheterization, a thin catheter is inserted via scleral incision and advanced posteriorly toward the target region for drug delivery,[4,9] while microneedle-based injection can be carried out using a short needle.

A clinically tested SCS Microinjector (Clearside Biomedical, Alpharetta, GA)[10] has been designed to introduce drug directly into the SCS, providing targeted and compartmentalized delivery to chorioretinal tissues, thereby optimizing local drug bioavailability and avoiding migration to the anterior segment and unwanted intravitreal dispersion.[11,12] The SCS ends anteriorly at the scleral spur, preventing fluid introduced into the SCS from spreading anteriorly. Hence, the fluid introduced into this region is driven by an anterior–posterior pressure gradient within the space relative to the IOP.[4,13] Optical coherence tomography imaging has demonstrated expansion of the SCS after injection in preclinical studies and in human clinical trial subjects,[14–16] supporting the SCS as a potential space and the directional flow of injected fluid from anterior to posterior. Choriocapillaris pore size, with an upper limit of 6 nm to 12 nm,[11,17] can also play a pharmacokinetic role in reducing rapid clearance in targeted tissues by limiting diffusion of introduced molecular suspensions, gene therapy viral vectors, or virus-like drug conjugates into the systemic circulation.[6,18] Preclinical studies of distribution and durability have reflected favorably on SCS injection. Animal eye models show high levels of small molecule injectates in posterior tissues including the retinal pigment epithelium and retina, and low levels in anterior structures.[3,6,19–21] In one preclinical trial, therapeutic levels of the small molecule tyrosine kinase inhibitor axitinib persisted in the retinal pigment epithelium–choroid–sclera and retinas of rabbit eyes 6 months postinjection into the SCS, demonstrating durability and supporting the potential for prolonged drug bioavailability.[20]

Triamcinolone acetonide suspension administered via SCS injection (XIPERE, Clearside Biomedical; Bausch + Lomb, Bridgewater, NJ) was the first therapy approved for suprachoroidal use, with an indication for uveitic macular edema. Clinical trials support the efficacy and safety of this formulation and mode of administration in this patient population.[2,5,11,22] Safety evaluation of suprachoroidal triamcinolone acetonide injection has shown low IOP-related adverse event (AE) rates with no serious ocular AEs out to 24 weeks.[23–25] Other suprachoroidally administered therapies being studied in clinical trials include CLS-AX (axitinib injectable suspension, a tyrosine kinase inhibitor with pan-vascular endothelial growth factor (VEGF) inhibition; NCT04626128) for macular degeneration, RGX-314 (adeno-associated virus-based gene therapy; NCT05407636, NCT04567550) for macular degeneration and diabetic retinopathy, and belzupacap sarotalocan (virus-like drug conjugate, AU-011; NCT04417530) for ocular oncology indications such as choroidal melanoma (Figure 2). These and other studies highlight the ability of SCS injection to accommodate various drug solutions and therapeutic agents, including gene therapy, virus-like drug conjugates, suspensions (which can be administered without a snow globe effect),[1] hydrogels,[26] and sustained release microspheres.[27]

Panel Methodology

Guidelines were developed based on a live panel discussion of the main topic areas—rationale for SCS injection, patient considerations and expectation setting, pre- and peri-injection management, injection technique, postinjection management, and follow-up—and review of published preclinical and clinical data. During the live discussion, the panel defined initial points of consensus and points for which additional clinical evidence is required to support further consensus. Initial conclusions for each of the predefined categories were summarized and subsequently reviewed and discussed by the panel in light of clinical experience and evidence to establish current, evidence-based guidelines for in-office SCS injection (Table 1).

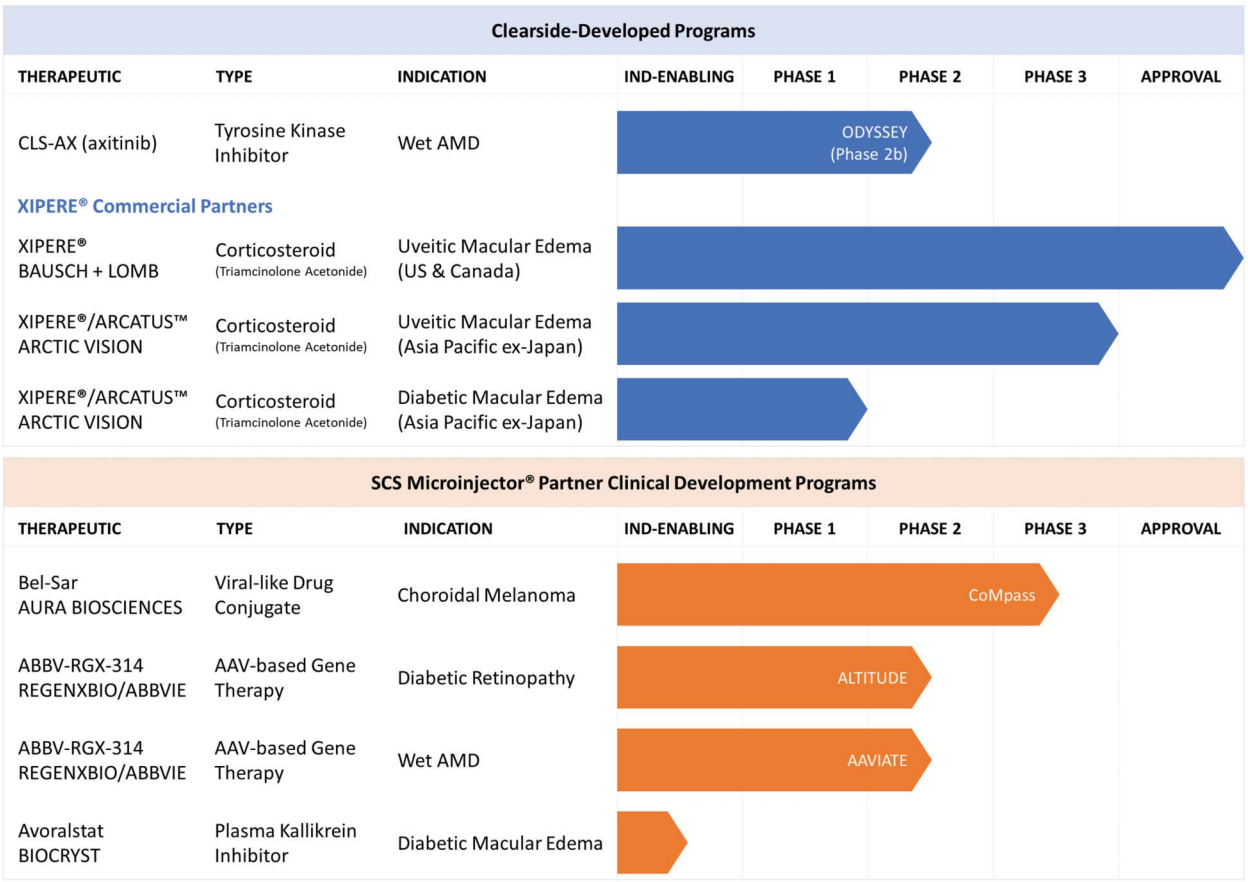

Fig. 2. Overview of clinical programs evaluating therapeutic agent delivery using the SCS Microinjector. Reproduced with permission from Clearside Biomedical, Inc.

Suprachoroidal Space Injection Guidelines

General Patient Considerations

Guideline: The decision to perform SCS injection should be based on individual patient considerations and clinical evidence. Because these populations were excluded from clinical trials, physicians should use their best clinical judgment when considering injection in patients with a history of ocular diseases such as glaucoma, hypotony, high myopia, abnormal axial length, scleral thinning, or abnormal lens status, or a history of procedures such as trabeculectomy, glaucoma shunt, or recent cataract or retinal surgery.

Before SCS injection, the physician should establish patient expectations for the procedure, including for patients who have previously undergone IVT injection. It is important to explain the injection sensation (which can be described as a transient, mild "pressure wave" due to the expansion of the SCS), longer duration of injection versus IVT, possible needle or injection site change during the procedure, and immediate postinjection and postdischarge monitoring and follow-up (Table 2).

Comment: Clinical evidence indicated a relatively low risk of AEs with SCS injection. Data from a total of eight Phase 2 and 3 clinical studies of suprachoroidally administered triamcinolone acetonide in 626 patients[28,29] show low rates of cataract and IOP elevation, no cases of endophthalmitis, scleral abscess, or suprachoroidal hemorrhage, no serious AEs related to lens injury, one serious AE of retinal detachment deemed unrelated to treatment by the investigator, and three serious AEs of vitreous hemorrhage unrelated to treatment.[23–25,29–31] Acute eye pain (defined as occurring on the day of the injection procedure and resolving the same day) has been reported in 3% of patients who received triamcinolone acetonide suprachoroidal injection in clinical trials,[32] a rate consistent with registration trials for intravitreal implants and IVT anti-VEGF agent injection.[33–35]

While a history of myopia or glaucoma, for example, was not an exclusion criterion in triamcinolone acetonide clinical trials, patients with high myopia (≥-6.00 diopter [D]), scleral thinning, or IOP >22 mmHg were excluded. Active ocular disease

Table 1. Summary of Areas of General Panel Consensus for SCS Injection and Areas Requiring Further Clinical Evidence

Points of panel consensus
Establishing patient expectations regarding procedure duration, sensation, potential for injection site and/or needle switching, potential risks, and monitoring
Positioning patient supine with adequate head and neck support and use of sterile speculum to prevent contact between eyelids and lashes and injection site
Use of sterile gloves, draping, and mask wearing during the injection procedure is optional and may be considered in accordance with office protocols
Use of local anesthetic to reduce patient discomfort and use of topical antimicrobial (povidone-iodine, 5%) at injection site and adjacent ocular structures before injection
Selection of 900-μm needle and injection site in the superior temporal quadrant, unless dictated otherwise by patient history, ocular anatomy, or clinical diagnosis
Injection using two hands, with positioning of needle perpendicular to the ocular surface and application of stable, firm pressure to ensure access to the SCS
Postinjection monitoring per standard office protocols for intraocular injection
Points for further clinical investigation
Selection of specific local anesthetic
Potential benefits of pupil dilation in SCS injections, specifically (i.e., for postinjection monitoring, prevention of inadvertent IVT injection)
Specific criteria for quadrant or needle switching (i.e., number of attempts with a 900-μm needle, quadrant selection)
Use and safety of SCS injection in special populations (i.e., high myopes, who may have scleral thinning, concomitant anticoagulant users, patients with IOP >22 mmHg, history of recent cataract or retina surgery, trabeculectomy, scleral buckle, or plaque radiotherapy)
Potential risks and recommendations for inadvertent IVT injection

such as scleritis or infection, uncontrolled relevant systemic disease, and history of pars plana vitrectomy surgery, scleral buckling, trabeculectomy or glaucoma shunt, or plaque radiotherapy were also noted as clinical trial exclusion criteria. Thus, additional real-world studies in these populations are warranted.

Guidelines for Pre- and Peri-Injection Management

Clinical setting. **Guideline:** Suprachoroidal space injections may be safely performed in an office setting.

Comment: Trials assessing SCS injection were completed in the office setting, and the data support the efficacy and safety of triamcinolone acetonide administered via SCS injection.[23–25] In a survey of experienced physicians participating in SCS injection trials with triamcinolone acetonide, 84% indicated that they did not perceive SCS injection to be meaningfully more difficult than IVT injection, with a majority reporting no new challenges with this technique.[36]

Bilateral injection. **Guideline:** Same-day bilateral SCS injection is appropriate, per physician judgment, with both eyes treated as separate procedures with different vials of medication and different injecting devices.

Comment: When performing same-day bilateral SCS injection, the panel agreed that each eye should be considered a separate procedure, with preparation, injection, and postinjection steps completed for the first eye, and then subsequently for the second eye. This should include a new microinjector, needle, and injectate vial, along with new gloves and draping, if being used.

Gloves, draping, talking, and mask use. **Guideline:** Sterile gloves, draping, and mask wearing during the SCS injection procedure are not necessary but can be used in accordance with office protocols. Although evidence is not unanimous, limiting talking during the procedure and/or wearing a mask may help reduce the spread of aerosolized oral contaminants and should be implemented when possible.

Comment: The panel's perspective on the optional use of sterile gloves, draping, and masks during injection is based on current evidence and is comparable with IVT injection evidence and guidelines.[37]

Table 2. Topics for Doctor–Patient Discussion to Establish Patient Expectations for SCS Injection

Duration of injection: SCS injection procedure is longer than IVT injection
Subjective sensation: it can be helpful to describe the subjective sensation as a "pressure wave" and acknowledge the differences relative to IVT injection sensation (possible temporary, mild discomfort due to SCS expansion)
Potential for quadrant and needle switching or multiple attempts to inject at the chosen injection site, which can prolong procedure duration
Need for routine postinjection monitoring procedures to confirm successful, targeted SCS injection and absence of acute adverse events before discharge
Signs and symptoms of complications to be aware of following discharge

Patient positioning. **Guideline:** Suprachoroidal space injection should be performed with patients in a relaxed, supine position with adequate head support.

Comment: Supine positioning can help limit movement during SCS injection and was recommended by the panel, particularly as physicians gain experience with the procedure. If the physician's experience is that SCS injection can be performed more efficiently and comfortably with the patient in an upright position, the panel noted that this may be done at the physician's discretion.

Local anesthetic use. **Guideline:** Topical or injection-based anesthetic selection can be based on physician preference and may include topical drops, lidocaine-soaked pledgets, gel, or subconjunctival anesthetic. If opting for subconjunctival anesthesia, the location of administration should be slightly removed from the planned location of SCS injection, due to the possibility of subconjunctival hemorrhage or conjunctival chemosis with resulting obscuration of procedure landmarks.

Comment: The IVT injection literature indicates no meaningful differences related to local anesthetic choice.[37] Given the potential for more complete anesthesia, it may be helpful to administer subconjunctival anesthesia for the first few patients requiring SCS injection while establishing familiarity with the procedure. There was general agreement among panel members that gel anesthesia may limit contact between the povidone-iodine and the conjunctival surface.

Use of povidone-iodine antiseptic. **Guideline:** Use of local antiseptic is highly recommended before SCS injection to minimize risk of infection. Before or after sterile marking of the initial or any subsequent injection site, povidone-iodine (5%) solution should be applied to the conjunctiva at the planned injection site and periocular skin and eyelid.

Comment: Povidone-iodine is strongly supported over topical antibiotics in the IVT injection literature[37] and was the most commonly applied antimicrobial in the clinical trials of suprachoroidally injected triamcinolone acetonide. After application of povidone-iodine, eyelid margins and lashes should not come into contact with the injection site (via the use of a sterile speculum) until the injection procedure has been completed. Povidone-iodine may also be applied to the eyelid margins, lashes, and periocular skin. For patients with povidone-iodine allergy, aqueous chlorhexidine may serve as a substitute. If using a gel anesthetic, povidone-iodine should be applied before and after gel application. The panel also noted that it may be beneficial to remove the gel anesthetic from the planned injection site before povidone-iodine application to ensure contact with the ocular surface.

Pupil dilation. **Guideline:** Pre–SCS injection pupil dilation is not essential, but dilation may be carried out per physician preference to support postinjection monitoring.

Comment: Pupil dilation may support observation for inadvertent IVT injection, which is rare (post hoc data from two Phase 3 trials of SCS triamcinolone acetonide given concurrently with IVT anti-VEGF therapy [NCT02980874; NCT03203447] reveal intravitreal delivery in 7/860 [0.81%] SCS injections [Clearside Biomedical, Inc, data on file]), evaluate the optic nerve head, and confirm absence of retinal tear or detachment, vitreous hemorrhage, or other AEs.

Globe softening. **Guideline:** Globe softening via gentle massaging or application of soft pressure to the globe before SCS injection is not required but may be used per physician discretion. It may be considered for patients with advanced glaucomatous optic neuropathy, patients at high risk of prolonged postinjection IOP spike (e.g., patients with high baseline IOP), or patients for whom any given IOP spike may result in damage to the optic nerve.[37]

Comment: Globe softening recommendations for SCS injection were noted in accordance with general IVT injection guidelines.[37] The use of globe softening to facilitate IVT injection, although uncommon, is an accepted practice.[37] The panel recommended limiting such massaging to the globe and application of soft pressure to the globe itself, and not the eyelids or ocular adnexa due to the possibility of bacterial spread onto the planned SCS injection site, which might theoretically increase the risk of infection.[37] Because globe softening may potentially make the injection more difficult, the use of glaucoma drops to reduce IOP before SCS injection may also be considered. It was also noted that performing an SCS injection in a hypotonic eye may be more difficult to complete.

Use of sterile speculum. **Guideline:** Even if a lid speculum is not routinely used for anti-VEGF IVT injections, use of a sterile lid speculum is recommended during SCS injection, given the longer duration of injection compared with IVT procedures (5–10 seconds per eye vs. approximately 1 second, respectively), need to use two hands for injection, importance of preventing contact between the eyelids, lashes, and injection site after antiseptic application and during injection, and because multiple injection attempts may be necessary to successfully complete the procedure.

Comment: While deemed less critical for IVT injection, the use of a sterile speculum was recommended by the panel for SCS injection. This was due to the

need to prevent contact of the eyelids and eyelashes with the injection site after antimicrobial treatment over a longer period of time versus IVT injection.

Initial needle length and injection site selection. **Guideline:** The SCS injection quadrant should be selected to optimize visualization and surgical approach and to help minimize the need for needle switching. The 900-μm SCS Microinjector needle and the selection of an injection site in the superior temporal quadrant are appropriate for most patients.

Comment: Analysis of injections performed in triamcinolone acetonide clinical trials indicates that using the 900-μm needle and targeting the superior temporal quadrant for the first injection attempt is adequate for accessing the SCS in the majority (78%) of patients,[36] although alternatives (such as the inferotemporal quadrant) may be considered based on physician judgment. No statistical correlations have been found between needle length and age, race, ocular disorder, refraction, visual acuity, IOP, retinal central subfield thickness, or lens status.[11,36] Injection site choice may vary depending on the indication, diagnosis, and reasons for SCS injection. For example, in the case of belzupacap sarotalocan (AU-011), an investigational therapeutic for choroidal melanoma, the ideal injection site would likely be in the two quadrants closest to the tumor location (two separate injections are given per treatment day). To increase success in accessing the SCS and limit the need for an injection site or needle switching, a site 4 mm to 4.5 mm posterior to the limbus should be selected[32] given the relatively uniform scleral thickness in this region.[38] This distance is slightly farther from the corneascleral limbus than the distance typically utilized during IVT injection procedures. In addition, the pars plana is posterior to the scleral spur and ciliary body but anterior to the retina's ora serrata, which limits potential risk to these structures.

Guidelines for Injection Procedure and Technique

Injection guidelines were aligned with clinical trial protocols and current labeled instructions for suprachoroidally administered triamcinolone acetonide regarding vial and microinjector preparation and injection technique,[32] although physician judgment and experience can be used to support injection success.

Suprachoroidal space microinjection preparation and technique. **Guideline:** The panel recommends performing SCS injection as follows (Figure 3). For drugs in suspension, the vial should be prepared per the prescribing information, including vigorously shaking for 10 seconds to adequately resuspend drug particles and prevent SCS Microinjector needle clogging. The SCS injection should be performed without delay to minimize the settling of the drug product in the syringe. After loading injectate into the SCS Microinjector and expelling air bubbles, the 900-μm needle should be connected in most cases.

After confirming and marking the injection site, one hand should be used to hold the clear barrel of the device and align the SCS Microinjector perpendicularly to the ocular surface at the injection site. The physician should then insert the needle through the conjunctiva and into the sclera. Ensuring contact between the needle hub and conjunctiva, stable, firm pressure should be applied with the needle hub, such that a dimple is formed within the conjunctiva and sclera on the ocular surface.

While maintaining this dimple and perpendicular positioning, the second hand should be used to depress the plunger of the SCS Microinjector to slowly introduce the prescribed dose volume of the injectate over 5 seconds to 10 seconds into the SCS. Suprachoroidal space injection should be performed more slowly than IVT injection, allowing the potential space of the SCS to expand and allow the injectate to flow posteriorly and circumferentially, minimizing the risk of reflux and patient discomfort. In the event of resistance, the positioning of the device should also be evaluated to ensure perpendicularity with the ocular surface. Reattempting injection at a different site or switching to the 1,100-μm needle should be considered at the physician's discretion. After the injection is completed, the needle hub should be held in place (without withdrawing) against the ocular surface for 3 seconds to 5 seconds and then removed slowly, with immediate application of a sterile cotton swab to the injection site with light pressure for 3 seconds to 5 seconds to facilitate spread of the injectate posteriorly and to minimize reflux of the injectate.

Comment: Suprachoroidal space Microinjector needle length is designed to approximate the thickness of the sclera while accommodating patient-to-patient variation in ocular anatomy.[38] Access to the SCS, therefore, requires correct injector positioning perpendicular to the ocular surface, and the application of sufficient pressure to create a dimple on the ocular surface with the needle hub. Movement of the plunger during injection should be felt as a loss of resistance as the injectate moves into the SCS. Resistance to injection or difficulty advancing the plunger can indicate that the SCS has not been accessed and that the needle is located in the sclera, and it is not recommended to use excessive force to deliver the injectate. If continued resistance is felt and the plunger does not advance, the physician should verify there is firm contact between the needle hub and

Fig. 3. Flowchart of suggested preparation procedure and recommended SCS injection sequence. Blue boxes indicate preinjection steps, orange indicates injection procedure steps, and green indicates postinjection steps. *Drug should only be shaken in the case of triamcinolone acetonide suspension (XIPERE; Clearside Biomedical, Inc; Bausch + Lomb) or other drug suspension, as described in prescribing information or clinical trial documentation. Shaking of gene therapy agents may either be unnecessary or detrimental.

ocular surface and perpendicular orientation of the SCS Microinjector to the surface of the eye. If these are confirmed and resistance is still felt that prevents successful SCS delivery, the plunger should not be forced, but rather switching to the 1,100-μm needle or attempting injection in a different quadrant should be considered.

Guidelines for Quadrant or Needle Switching

Guideline: Steps can be taken to limit the need for needle switching. If injectate cannot be introduced into the selected injection site with the 900-μm needle, the physician may first adjust the positioning of the device to ensure true perpendicularity with the ocular surface at the site of injection and that a dimple is present at the ocular surface. If an injection still cannot be performed, switching to the 1,100-μm needle and reattempting injection in the same quadrant can be considered. If clinical judgment indicates a need to switch to the 1,100-μm needle, the 900-μm needle should be removed, the SCS Microinjector syringe reconnected to the injectate vial and reloaded per the steps defined above, and the 1,100-μm needle attached. Sterile preparation of the ocular surface should be repeated, with reapplication of povidone-iodine, and repeating of the injection technique described. If switching quadrants, the panel recommended considering repeating all preparation steps for the new quadrant (see *Guidelines for Pre- and Peri-Injection Management*) (Table 3) and performing the injection in the new quadrant with the 900-μm needle. The needle and quadrant used for each eye can be noted in the patient's chart for future reference.

Comment: During injectate loading, air bubbles should be expelled by sliding the plunger back and forth. Once all air bubbles are eliminated, the plunger is advanced so that its tip aligns with the required syringe volume. The SCS injection should be performed with minimal delay after this step to avoid drug settling within the SCS Microinjector. The panel noted that there is currently no data to inform on the number of injection sites that should be attempted with the 900-μm needle before switching to the 1,100-μm needle, nor the number of times injection in a given quadrant should be attempted before switching to another quadrant. In light of the absence of evidence, the decision to switch quadrant and/or needle should be based on clinical judgment and the goal of limiting patient discomfort. The sclera is thickest posteriorly (996 $\pm$ 181 μm) and thinnest equatorially (491 $\pm$ 91 μm), with some variation between quadrants.[38] Analysis of data from six clinical trials with suprachoroidal triamcinolone acetonide showed that 78% of injections in the superotemporal quadrant were completed with the 900-μm needle (vs. 65% in the inferotemporal quadrant), and fewer female than male patients required the use of the 1,100-μm needle (24% vs.

Table 3. Guidelines for Quadrant or Needle Switching in SCS Injection

Initial recommendation is to use the 900-μm needle* and select an injection site in the superior temporal quadrant 4–4.5 mm posterior to the limbus, as measured with the caliper feature of the needle cap or standard ophthalmic calipers†. If a 900-μm needle is not adequate for injection at the selected injection site, consider an alternative quadrant for injection and repeat all preinjection steps
If a needle switch is required, the 900-μm needle should be removed, the SCS Microinjector syringe reconnected to injectate vial and reloaded, and the 1,100-μm needle attached
Patient should be given a "break" (if needed) between injections to ensure patient positioning and relaxation for injection and appropriate repreparation of the ocular surface and reloading and preparation of the SCS Microinjector
Aseptic technique should be utilized for needle or quadrant switching

*Unless the 1,100 μm is more appropriate based on ocular anatomy or other clinical factors.
†Injection quadrant should be selected to minimize changes of needle switch requirement. All regions can be considered based on physician judgment.

34%).[36] Applying slightly greater pressure with the needle on the ocular surface may compress the sclera and increase the success with the 900-μm needle before switching to the 1,100-μm needle. It is important to remind patients that a need to switch the injection site or needle may extend the time for successful procedure completion.

Guidelines for Postinjection Management and Follow-Up

Postinjection monitoring. **Guideline:** Post–SCS injection monitoring, including evaluation of IOP and general ocular function, should be in accordance with standard office post-intraocular injection protocols and product prescribing information.

Comment: Potential IOP increases, both transient and sustained, can be associated with IVT injection[37] and with the administration of corticosteroids. Therefore, these should be monitored following SCS injection. The panel noted that larger injectate volume, whether introduced into the vitreous or SCS (0.1 mL vs. 0.05 mL), can be associated with greater IOP increase immediately postinjection. If IOP is sufficiently elevated to impair vision or optic nerve perfusion, anterior chamber paracentesis may be needed. In cases with lower IOP elevation, the eye should be carefully monitored for vision and/or IOP normalization.

Data are insufficient to inform specific recommendations regarding monitoring and treatment related to potential inadvertent injection into the vitreous.

Patient discharge and follow-up. **Guideline:** Suprachoroidal space injection recipients and their caregivers should be informed regarding common or expected side effects following injection, such as subconjunctival hemorrhage, as well as signs and symptoms of more serious potential complications such as infection, retinal detachment, or suprachoroidal hemorrhage, which could theoretically develop after SCS injection. Patients should be provided with 24-hour contact information to report concerning signs and symptoms, including worsening vision, eye pain or discomfort, light sensitivity, redness, or loss of central or peripheral vision. Intraocular pressure elevation or complications like endophthalmitis or scleritis should be managed in accordance with standard protocols for postinjection patients.

Comment: The presence of clear vision, confirmed perfusion of retinal artery, and absence of acute complications are sufficient for patient discharge and may be confirmed before the patient leaves the office. All potential signs and symptoms noted above should be monitored, though, to date, data indicate low risks of AEs such as endophthalmitis after SCS injection.[23–25,29–31] Treatment-related acute complications with SCS injection were infrequent in clinical trials of suprachoroidal triamcinolone acetonide injection, with ongoing studies to provide insight into the safety of in-development therapeutics (CLS-AX, RGX-314, AU-011).[23–25,39,40]

Conclusions and Future Directions

The SCS injection procedure has been developed to provide targeted and durable retinal and choroidal drug delivery, and current evidence and clinical experience support its safe and effective implementation into routine clinical practice. Although this remains a relatively novel approach, these guidelines reflect current best evidence and experience of the expert panel regarding SCS injection.

Many opportunities remain for future investigation regarding SCS injection. Data to support more specific, defined approaches and criteria for quadrant and needle switching would be beneficial. In addition, the current clinical trial data on the efficacy and safety of SCS injection do not include (or include in small numbers) specific patient populations who may be eventual candidates for SCS therapeutic delivery, including patients with high myopia (≥-6 D) or scleral thinning, patients with IOP >22 mmHg, or those with a history of pars plana vitrectomy surgery,

scleral buckling, trabeculectomy or glaucoma shunt, or plaque radiotherapy. While ongoing studies using SCS injections will continue to inform our understanding of best practices for performing SCS injections, the guidelines presented in this review are intended to help improve the standardization of technique and the probability of safe and successful injection for patients.

Key words: drug delivery, intraocular injection, guideline, retina, suprachoroidal space, suprachoroidal injection, suprachoroidal administration.

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