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## Real World Trends in Intravitreal Injection Practices Among American Retina Specialists

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### Abstract

**Purpose:** To analyze practice patterns employed for intravitreal injections (IVI) by retinal specialists in the United States.

**Design:** Cross-sectional online survey.

**Participants:** Retina specialists in the United States who responded to a web-based survey.

**Methods:** Retinal specialists in the United States were contacted via email to complete a web-based, anonymous 24-question survey. Multivariate analysis was performed on a selected question of interest focused on choice of anesthetic used for IVI.

**Main Outcome Measures:** Differences in IVI practices, such as antibiotic preferences, and different odds of anesthetic use by demographic variables with 95% confidence intervals (CI).

**Results:** A total of 281 retinal specialists responded to the survey (17% response rate). Respondents had an average age of 53 years with an average of 20 years in practice. Respondents practiced in 42 states, with 90% practicing in an urban or suburban area. For anesthesia, 14% utilized a topical anesthetic with cotton swab compression, 27% a subconjunctival anesthetic, and 31% an anesthetic gel. Age, gender, geographic location, and practice setting did not appear to significantly impact choice of anesthetic for IVI. 66% of respondents always used a lid speculum,

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21% administered topical antibiotics prior to injection, 36% wore a mask, 73% wore gloves, and 45% always dilated the eyes prior to injection. The majority of respondents utilized a 30-gauge needle and injected in the inferior temporal quadrant (70%). 45% would always perform bilateral injections the same day if indicated. After the injection, 14% administered post op NSAIDs, 28% administered post-op antibiotics, and 31% routinely checked intraocular pressure after injection.

**Conclusions:** This study provides real-world trends in practices for IVI among retina specialists in the United States. In addition, age, gender, practice type, or geographic location did not influence anesthetic choice for IVI.

## Precis

This large survey of intravitreal injection practices among retina specialists in the United States illustrates current real world trends and preferences among retina specialists.

## Introduction

Intravitreal Injections (IVI) have now been accepted as the standard of care for delivering therapeutics to the retina. Since 2006, there has been rapid increase in the number of intravitreal injections, estimated to have been around 5.9 million in 2016.<sup>1</sup> There is a wide spectrum of approaches employed for preparation, technique, antibiotic usage, and post injection examinations for intravitreal injections.<sup>2,3</sup> These practices generally involve considerations for preventing endophthalmitis, improving patient comfort, and optimizing clinical workflow. The most concerning risk associated with IVI has been the development of endophthalmitis. Employing different techniques before, during and after IVI procedures, such as the decision to use povidone-iodine either in addition to or instead of prophylactic antibiotics, can affect the rates of endophthalmitis.<sup>4</sup> Additional complications of IVI include an elevated intraocular pressure, ocular hemorrhage, rhegmatogenous retinal detachment, and cataract formation.<sup>4-7</sup>

While various guidelines have been published by various groups for evidence based practices surrounding IVI, it is unclear how these practices are incorporated in the real world.<sup>2,3</sup> Furthermore it is unknown whether demographic characteristics, such as age, gender, or practice setting can affect certain practices, such as choice of anesthetic used for IVI. The purpose of this study is to survey current practices surrounding intravitreal injections in the United States and to analyze differences based on various demographic parameters for choice of anesthetic used in IVI.

## Methods

A subset of retina specialists in the United States were contacted via email to complete a cross-sectional 24 question, internet-based survey aimed at better understanding pre-procedure methodologies, materials used, medications used, and post-procedure protocols related to IVI. This subset was identified by cross referencing names from the American Society of Retina Specialists Find a Retina Specialist webpage (<https://www.asrs.org/find-a-specialist>) (USA as a search term) to contact information obtained from publicly available sources as well as other retina specialists.

The survey was created in the Qualtrics Research Core Platform, a web-based platform that allows data storage in a password-protected database and export data into CSV, PDF, and Powerpoint formats. The survey was entirely anonymous and thus no identifiable information was acquired or stored in the database and is compliant with current HIPAA guidelines. The first page of the survey was an informed consent page and required every participant to agree to the informed consent to be eligible to complete the survey. This research study has been certified as exempt from IRB review by the UC San Diego Human Research Protections Program and permits the administration of the web-based survey to retinal specialists. The research study adhered to the tenets of the Declaration of Helsinki.

On November 5<sup>th</sup>, 2018, emails were sent out to 1676 retina specialists in the United States, of which 34 emails immediately were returned. Thus, the survey was successfully sent out to 1642 participants, of which 281 completed the survey. Between November 5<sup>th</sup> and December 11<sup>th</sup>, two email reminders to complete the survey were sent to the retina specialists. The second email reminder stated that the survey would be closed within 7 days. The survey response collection was stopped on December 14<sup>th</sup>, 2018 and results were analyzed on December 17<sup>th</sup>, 2018.

For choice of anesthetic used for IVI, we used logistic regression to quantify and evaluate the relationship between demographic covariates and responses. Response to a question was treated as a binary (yes/no) with non-responders excluded from the analysis. All demographic covariates of interest were included in the multivariate regression, which include age, gender, geographic location, and practice setting. We reported odds ratios with relation to reference groups as discussed in the results section, as well as 95% confidence intervals and p-values using the Wald test. All statistics were performed using R version 3.5.2 (<https://cran.r-project.org/>).

## Results

### Demographics

There were a total of 281 individuals (17% response rate) who responded to the survey by the allotted deadline, which was stated in the final reminder email. Some of the respondents chose not to respond to select questions in the survey. The age range of respondents was 29 to 78, with an average age of 53. Eighty-five percent of respondents identify as male (240/281) and 13% as female (37/281). Among the respondents, 11% have been in practice between 0 and 5 years post-fellowship (31/279), 14% between 6 and 10 (39/279), 11% between 11 and 15 (32/279), 15% between 16 and 20 (41/279), and 49% for 21 or more years (136/279), with an average practice length of 20 years post-fellowship and practice length range between 1 and 46 years. In terms of geographic distribution, physicians from 42 different states responded to the survey, with the largest representation from California (15%, 41/274), Florida (9%, 24/274), Texas (7%, 19/274), and New York (7%, 18/274). Fifty-two percent of respondents categorized the setting of their practice as suburban (146/281), 42% as Urban (117/281), 5% as Rural (15/281) and 1% as other (3/281). With respect to practice setting, 40% work in a “Retina-only practice with greater than 2 retina specialists in the group” (112/280), 20% in a “Multi-specialty ophthalmology group” (57/280), 20% in an “Academic/University medical group” (56/280), 16% in “Solo or less than 3 retinal

specialists in a retinal only group” (45/280), and 4% in a “Large multi-specialty medical group” (10/280). Around half of the respondents perform between 30–80 IVI per week (138/281), 20% perform between 0 and 30 IVI per week (57/281), and 31% perform 80 or more IVI per week (86/281).

## Pre-Injection Procedures

The results for the pre-injection practices are detailed in Table 1. Briefly, seventy-two percent of respondents reported a nurse or assistant present in the room to help in preparation (20/281). There was a wide array of responses with respect to the type(s) of anesthetics used prior to injection. Among respondents, 16% reported using a topical anesthetic only (46/281), 14% using a topical anesthetic and cotton swab compression (40/281), 31% using an anesthetic gel only or in addition to a topical anesthetic (88/281), and 27% using a subconjunctival anesthetic only or in addition to a topical anesthetic (77/281). We then performed further a multivariate analysis looking specifically at this question of type of anesthetic used. The variables included in the analysis were age, gender, years practiced, geographic location, and practice setting. We did not find a statistically significant association of age, gender, years practiced, or geographic region on retinal specialists’ choice of anesthetic regimen for IVI ( $p>0.05$  for all variables and are available upon request).

The majority of respondents used a lid speculum every time they performed an IVI (67%, 187/281), while 22% never used one (62/281). In terms of applying betadine on the eye, 63% of respondents dropped betadine from a bottle (177/281). If a patient stated that they have a betadine allergy, 58% still used betadine as they believe the allergy did not exist (16/278), while 36% chose a strategy not offered in the choices (100/278). Among those who chose to handle the allergy with alternative means, 22% stated that they would administer antibiotics either before or after the injection (22/100), and 21% would minimize exposure of Betadine to only the injection site or by decreasing the concentration (21/100).

In other aspects, the majority used gloves every time (73%, 145/199) and swabbed eyelids and eyelashes with betadine every time (59%, 117/199). However, only 36% used a mask every procedure (72/199) and only 21% used topical antibiotics prior to injection (42/199). While 45% of respondents dilated the eyes prior to injection (127/281) every procedure, 37% only dilated the eyes half or less than half the time (104/281) prior to injection. The majority of respondents did not perform anterior chamber paracentesis for patients at risk for conditions such as Glaucoma (63%, 177/280).

## Injection Procedures

While the majority of respondents used a 30-gauge needle (61%, 170/279), 21% elected to use a 31-gauge needle (59/279) (Table 2). Most respondents injected in the inferior temporal quadrant (70%, 195/279), though 27% chose to inject in the superior temporal quadrant (74/279). If a patient required bilateral injections, 31% stated they would perform it on the same day in every situation (88/281), while 25% would never perform it on the same day (69/281). Most of the retinal specialists who responded did not measure the distance from

the limbus upon injecting (69%, 195/281), though 20% utilized calipers (55/281). There was a bimodal distribution on whether to place a cotton tip over the injection site immediately following injection. While 55% never placed a cotton tip immediately over the spot (153/281), 37% of respondents placed a cotton tip over the injection site every time (103/281).

## Post-Injection Procedures

Half of the survey respondents utilized Balanced Salt Solution (BSS) to irrigate betadine out of the eyes (50%, 141/281), while 30% chose “Other” means not listed (84/281), and 20% used 3mL 0.9% sodium chloride (56/281) (Table 3). Among those who chose other means, 35% of them used the commercially available “Eye Wash” solution (29/84). Among respondents, 31% stated that they routinely checked IOP (38/123), 28% routinely administered a topical antibiotic (34/123), and 46% routinely performed “Other” procedures post-injection (57/123). Among those that responded “Other,” 21% checked for visual acuity in some manner (counting fingers, hand motion, etc) (12/57).

## Discussion

The number of intravitreal injections performed each year continues to increase as the prevalence of retinal vascular diseases such as age-related macular degeneration (AMD), diabetic retinopathy, and retinal occlusion continue to grow. While a number of previous surveys of IVI practice have been performed, to the best of our knowledge, this is the largest survey that has been performed that details the specific anesthetic agents, antibiotic usage, and various other techniques employed while performing IVI. In particular, in the United States, the last survey was conducted in 2011 by Green-Simms et al.<sup>2</sup> A more recent survey detailing IVI techniques was conducted in Israel in 2016 as well.<sup>8</sup> We also reviewed the results from the last five years of the PAT survey from the American Society of Retina Specialists (2014–2018), and only 6 questions over the entire 5 years overlapped with questions in the survey. Though these surveys have assessed important information about best practices for IVI, they do not detail important information regarding specific anesthetics used, betadine allergies, nor assess differences in techniques based on demographic parameters. In this study we performed additional multivariate analysis to assess the effect of demographic variables on anesthetic choice for IVI, and did not find that age, gender, practice type, or geographic location influenced anesthetic choice for IVI.

## Pre-Injection Methodology

The study found that the majority of respondents had a nurse or assistant present in the room to help prepare for the injections, which can lead to increased efficiency and decreased errors in preparation.<sup>9</sup> Interestingly, anesthetic choice did not differ based on gender, age, practice setting, or geographic location. Previous studies have not demonstrated a significant difference in pain score between the different types of anesthetic used for IVI<sup>10,11</sup>.

The majority of respondents utilized a lid speculum, which can help to avoid lid reflex closure and subsequent exposure of microbes to the injection site. For those respondents that

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