Meeting Notes from the 42nd Annual Meeting of the ARDS

As a service to our readers, Retina Today is pleased to present the following brief summary of selected lectures at the 42nd Annual Meeting of the Aspen Retinal Detachment Society (ARDS).

The ARDS offers attendees a variety of long-form lectures on important topics in surgical and medical management of the retina. The format allows leading experts time and space to update the audience on the nuances of the important topics they encounter in the clinic on a daily basis. Yet, far from being a didactic encounter, the real value of the ARDS is in its interactive format. Dynamic discussion among participants is in fact the hallmark of the ARDS, whether those discussions take place in the meeting room, in the hallway between talks, or on the nearby ski slopes.

The stated goal of the ARDS is to offer attendees a format in which they can enhance competency in the fields of vitreoretinal diseases, surgery, and practice management. The ARDS CME Program includes scientific paper presentations and panel discussions from world-renowned vitreoretinal specialists.

The upcoming 43rd Annual Meeting of the ARDS will take place from February 28 to March 4, 2015. More information about the meeting may be found at http://www.medconfs.com/conferences.php..

Future OCT Imaging

Srinivas R. Sadda, MD

"What can't we do with OCT that we would like to do?" Srinivas Sadda, MD, asked in a talk exploring the future applications of optical coherence tomography (OCT) imaging, Although OCT capabilities have advanced significantly from the era of time-domain algorithms, fourier-domain principles do not solve certain inherent instrument limitations. For instance, Dr. Sadda said, the light sources used in commercially available OCT devices are limited in their ability to penetrate the retinal layers, and therefore, there is not an ability to see cellular level detail. Even though spectral-domain (SD) OCT can achieve faster scans than time-domain platforms, it still yields only anatomic data, and so there is little to glean in terms of functional information. Thus, Dr. Sadda said, despite the utility of OCT in the clinic, there is, in fact, significant opportunity to improve the quantitative information available from OCT images.

Adaptive optics platforms currently in research labs may contribute an ability to delve deeper into the retinal and choroidal layers, perhaps revealing new pathologic understandings and altering clinical decision making. Although newer light sources using different bandwidth and wavelength light may further enhance axial resolution, "improving axial resolution may not buy us that much in enhancing the care of our patients. ... Where we really need improvements is in transverse resolution," Dr. Sadda said.

Perhaps the most important development, Dr. Sadda said, is swept-source (SS) OCT. "One of the great advantages of swept source is that it is faster than spectral domain," Dr. Sadda said, "but one of the even bigger benefits is that it offers greater sensitivity with less loss of sensitivity in depth."

SS-OCT may ultimately expand the role of imaging in

the management of retina disease. As Dr. Sadda pointed out, several papers have already been published looking at SS-OCT to image the vitreous, and several research teams are using SS-OCT in patients with uveitis in an attempt to quantify cells. SS-OCT also delivers more clear en face images that mimic fundus photographs; and, if SS-OCT is coupled with laser light sources (ie, 1050 nm wavelength), it could yield even greater penetration to retinal layers or perhaps be used to visualize the angle in the anterior chamber.

Another development in OCT technology being looked at is in the ability to extract functional data from static or serial images. OCT angiography is an example of this emerging integration of advanced software processing and improved imaging hardware.

Macular Degeneration: Things You Did Not Know

Thomas R. Friberg, MD

Despite extensive research and release of new information about drusen morphology and impact in recent years, there remain many unanswered questions regarding their role in the progression of age-related macular degeneration (AMD) and the development of geographic atrophy.

In a talk highlighting recent studies on drusen, Thomas Friberg, MD, pointed out what is generally accepted regarding drusen: that they represent depositions on the surface of the retina pigment epithelium and Bruch membrane, thus insulating Bruch membrane from the choroid and affecting nutritional pathways. Yet, when patients present in the clinic with multiple or enlarged drusen, the clinical relevance of these findings is largely unknown, he said.

Studies attempting to affect better outcomes via elimination of drusen have not shown a benefit. In a study that Dr. Friberg was involved with, the delivery of laser treatment to drusen imparted no protective effect in the development of geographic atrophy compared with observation (ie, no treatment). Additionally, eyes with choroidal neovascularization (CNV) in 1 eye that received laser in the other eye intended to eliminate drusen wound up doing worse than eyes that were observed.

Dr. Friberg also presented findings from a study seeking to discern if drusen could be used as a variable in quantifying the risk for CNV development. The study showed that "larger drusen area does not necessarily impart a greater risk for CNV to the eye." Further analysis revealed that increasing numbers of drusen do increase the risk of neovascularization up to a point, but after that point, there is no greater risk. What that threshold number is, however, is unknown.

Change in drusen area does not appear to affect CNV risk, but when coupled with visual acuity data, there may be clinical relevance in tracking change in drusen area. According to Dr. Friberg, patients with poorer vision have a poorer prognosis, and thus, patients with poor vision and marked changes in drusen area may require closer monitoring for development of CNV.

Is Fluorescein Angiography Still The Gold Standard For Diagnosis Of Neovascular AMD?

Ramin Tadayoni, MD, PhD

The role of fluorescein angiography in the diagnosis of AMD remains a controversial topic. The technology is much more widely used in Europe, whereas American retina specialists more typically rely on SD-OCT as a diagnostic and monitoring tool. According to Ramin Tadayoni, MD, PhD, there may be benefits and disadvantages to relying solely on one or the other device.

Each platform has pluses and minuses, according to Dr. Tadayoni. Namely, fluorescein angiography is useful for depicting vascular characteristics and the topography and area covered by CNV, but it does not show where the vessels are beyond the RPE and it does not show the secondary damage they may cause. Meanwhile, SD-OCT clearly depicts the retina, but not so much the CNV vessels; it shows RPE elevation, retina edema, and exudative detachment and it is very relevant for depicting response to anti-VEGF treatment, but it may not be particularly good for the primary diagnosis and classification of AMD.

Dr. Tadayoni presented the results of a study he led to determine the best combination of imaging to make the diagnosis of CNV in AMD. A team of experienced retinal specialists were supplied images from fluorescein angiography and SD-OCT in a blinded fashion. About a third of eyes enrolled in the study had classic lesions, a third had occult, and about a third were mixed. In the end, sensitivity and specificity of fluorescein angiography was about 90%; SD-OCT achieved comparable sensitivity and specificity.

Where the 2 modalities differed, however, was in subgroup analysis by type of lesions. All classic lesions were diagnosed properly with both fluorescein angiography and OCT. All the errors in diagnosis, Dr. Tadayoni said, occurred in eyes with either occult or mixed morphology. Even further, small lesions were more likely to be missed, and the experience of the graders might have affected the accuracy of the diagnosis—more experience with imaging may yield more accurate results. Finally, Dr. Tadayoni noted that review of the entire SD-OCT study was associated with significant increased sensitivity and specificity for evaluation of the individual patient compared with review of "selected" SD-OCT images.

Latest Observations on Widefield Imaging of Retinal Diseases

Szilárd Kiss, MD

The number of research studies looking at widefield imaging has exploded in recent years, but "is there any clinical utility in looking beyond the 30-50° of focus of typical OCT?" asked Szilárd Kiss, MD.

In fact, there may be. According to Dr. Kiss, although the

fovea and macula are the primary source of pathology for most diseases treated by retina specialists, there are diseases that are present only in the periphery, and peripheral findings may be indicative of or may contribute to center-involving pathologies like AMD and diabetic macular edema



(DME). Thus, he said, widefield imaging is *becoming* a standard in retina practice, although it may not affect clinical decision making until more studies are conducted.

Currently, 2 devices are available for imaging of the peripheral retina: a lens affixed to a Heidelberg platform or the Optos platform, which is a mirror-based system. In a study of 10 eyes of 5 patients headed by Dr. Kiss, the Optos platform imaged more of the overall retina than a Heidelberg Spectralis. Both devices delivered images that exceeded the standard 7 ETDRS fields; the Spectralis imaged more of the vertical axis (the inferior and superior regions), and the Optos delivered images further into the horizontal axis of the eye (the nasal and temporal regions).

Regardless of individual pros and cons, all widefield imaging devices are prone to distortion and nonlinearity errors, said Dr. Kiss. Whenever you project a 3-dimension image on flat surface, there will invariably be distortions in the periphery—in a similar fashion to the way a flattened map of the



world depicts Greenland as the same size as Africa, despite that the latter is 14 times larger than the former. In the clinic, Dr. Kiss said, this may lead to incorrect assumptions about peripheral pathology, such as the size of the nevi.

Dr. Kiss concluded his talk discussing ongoing research on the use of widefield imaging in diabetic retinopathy. The standard 7 field ETDRS montage captures about 180° of the retina, but there may be implications for findings in the periphery, and the standard 7 fields may be insufficient for classifying some cases of diabetic retinopathy. Early research has suggested that widefield imaging may be as good as the dilated fundus examination for classification and it "may ultimately change how we classify patients, and it may change how we treat patients."

Founders Lecture: Anti-VEGF Maintenance Therapy for Neovascular AMD

Carl D. Regillo, MD

Getting the macula dry in a patient with neovascular AMD is the easy part, the hard part is "what to do after," Carl D. Regillo, MD, said during the Founders Lecture.

Most patients are going to require long-term follow up with anti-VEGF injections because as effective as they are in helping to eliminate neovascularization, they are not curative, Dr. Regillo said. However, it is still unknown how to use anti-VEGF therapy over the long-term while balancing the sometimes conflicting elements of safety, efficacy, cost, and treatment burden (to physicians, patients, and the overall health care system).

There are 3 predominate clinical approaches to maintenance therapy, each with their individual pros and cons. Continuous fixed (monthly or bimonthly) injections is the most widely studied approach and it proved effective in

the major clinical trials that led to the approval of both ranibizumab (Lucentis, Genentech) and aflibercept (Eylea, Regeneron). But injecting monthly is largely unsustainable from a practical standpoint, and it likely leads to a significant amount of over



treatment in a majority of patients, thus adding extraneous cost to the care of patients with AMD and introducing unnecessary risks for the development of adverse outcomes.

Several studies have demonstrated that discontinuous variable therapy (PRN) based on the results of OCT imaging is effective. Although PRN therapy reduces the treatment burden associated with anti-VEGF therapy, patients still require monthly imaging visits. The downside of this treatment strategy, Dr. Regillo said, is the potential for recurrences, and multiple recurrence might lead to advancement of disease that "we are not able to recover from." The most popular approach is continuous variable or treat-and-extend (TAE) protocols. Dr. Regillo described the approach as proactive rather than waiting for a recurrence to retreat as with PRN. As well, TAE is individualized, so therapy is maximized in terms of safety and efficacy and is more cost effective (ie, reducing office visits, testing, etc.) than other approaches.

The American Society of Retina Specialists' Preferences and Trends Survey indicated that about 78% of retina specialists use TAE, but there have been no studies comparing it with other treatment algorithms, Dr. Regillo said.

Compounding Pharmacies and Endophthalmitis

Harry W. Flynn Jr, MD

Recent regulatory activity in response to highly publicized infectious outbreaks associated with compounding pharmacies has created some confusion for practicing clinicians, said Harry W. Flynn Jr, MD.

Dr. Flynn said that the safe use of compounded drugs relies on 2 critical steps being followed: (1) physicians should use a sterile set up for each medication delivered; and (2) the compounding pharmacy from which the drug originated should follow good practices and be in compliance with federal law (ie, compliance with standards and practices [US Pharmacopeia 797] and regulations within the Food, Drug, and Cosmetic Act and Drug Quality and Security Act 2013). But doctors can also be proactive in limiting their

liability: In his role as a consultant on compounding pharmacies to the US Food and Drug Administration, Dr. Flynn said he has seen a number of lawsuits arise because doctors did not provide a phone number to patients to call if symptoms developed after



an injection. Another often overlooked procedural step, he said, is to record the lot number of each dose, so that if an outbreak occurs, it can be traced, tracked, and analyzed.

Compounding pharmacies operating in the United States are bound by US Pharmacopeia 797, which although developed by an expert committee, is not based on data from clinical trials. The guidelines highlight important practices that must be followed: drug draws should be performed in a sterile room and all doses should be quarantined for 14 days and tested for microbial growth before they are released. A breakdown in these processes, Dr. Flynn said, is what leads to bad outcomes with compounded medicines.

The Food, Drug, and Cosmetic Act and Drug Quality and Security Act 2013 introduced measures by which compounding pharmacies can become certified by the Pharmacy Compounding Accrediting Board. The issuance of certification should be an indication that the pharmacy

takes additional steps to ensure the safety of its products, and it is meant to be an additional metric by which physicians can judge the quality of pharmacies, Dr. Flynn said. Interestingly, he noted, most of the outbreaks associated with compounding pharmacies have occurred in noncertified, non-Pharmacy Compounding Accrediting Board accredited compounding pharmacies.

There are safeguards physicians can use in the clinic to ensure the further safety of compounded doses. At his institution, Bascom Palmer, Dr. Flynn said every intravitreal injection is performed according to a standard protocol that involves the use speculum and gloves, 10% povidone iodine on lids and lashes, topical 5% povidone iodine to ocular surface for a minimum 30 second exposure, and a cotton swab soaked with 4% lidocaine with light pressure. Antibiotics are not used prophylactically. Dr. Flynn said this protocol, which costs about \$5 per use, is used for about 14 000 injections a year with a very low rate of endophthalmitis.

Local Risk Factors for the Development of Geographic Atrophy

Srinivas R. Sadda, MD

Geographic atrophy (GA) is considered the end stage of AMD, and so ongoing research about its etiology may help inform treatment, patients' education, and risk calculation, according to Srinivas R. Sadda, MD.

Different drusen morphologies may help predict which will go on to develop GA. Dr. Sadda presented results from a natural history study of drusen followed over 6 months. Drusen height did change (consistent with previous studies), and most of the atrophy events occurred in shrinking lesions. Thus, he said, a decrease in drusen may be an ominous finding. And yet, not all cases with decreasing drusen

develop atrophy. Further, atrophy was much more common in drusen with "dark spots" in them. In fact, drusen hyporeflectivity and pigment migration were the strongest predictors for the development of GA in the study.



Dr. Sadda offered a hypothesis based on the findings from the study: "If you have some small drusen, this might be normal aging. Once you get to medium drusen, then you may have some early AMD and you are on the path [to potentially developing GA]," he said. "Some people progress on and will develop intermediate AMD, but this is potentially still stable. On the other hand, once you develop pigment migration and hyporeflective drusen, these are really high-risk features. These may represent a critical hit: You may go on to develop a RPE disintegration, even if not a frank atrophy just yet, and then you wind up with atrophy."

The appearance of psuedodrusen, as identified in work

by Rick Spaide, MD, is another potentially confounding factor, Dr. Sadda said. Subretinal drusen deposits coalesce over time to form a sheet; that sheet disintegrates leading to photoreceptor atrophy in the absence of RPE atrophy, and so "Spaide showed there is a new atrophic pathway that was totally unrecognized in previous AMD studies," he said.

The Law of Unintended Consequences in Health Care Reform

David W. Parke II, MD

Any time big changes are enacted upon complex systems, there will inevitably unintended consequences to those actions—and sometimes they are good but often they are negative. According to David W. Parke II, MD, recent changes in health care policy—and not just the ones resulting from the Patient Protection and Affordable Care Act—will invariably change how retina specialists practice.

Dr. Parke highlighted the ongoing struggles with the Sustainable Growth Rate (SGR) formula, the measure enacted as part of the 1997 Balanced Budget Act that ensured "annual increase in expense per beneficiary did not exceed

the GDP," Dr. Parke Said. "In fact, it was GDP plus 1. If it did [exceed the GDP], the conversion factor would change the next year to try and bring things back under control."



Between 2003 and 2014, 16 separate laws were passed to prevent the

"SGR cliff" from falling over, but this built up a debt of about \$140 billion. The expense per beneficiary has had a 0.29% average annual update over that time; however, practice costs rose 26% and actual inflation adjusted payments went down 17%, Dr. Parke said.

On the positive side, the average salary for ophthalmologists has risen about 3% per year despite lower adjusted payments, primarily because of new procedures and greater volume. However, Dr. Parke said, physicians face a decrease from value based payment of 8% cut by 2016 from Physician Quality Reporting System and resource-use based modifier (ie, the value based modifier)—meaning that, all tolled, physicians face a potential 15% drop in reimbursement by 2017.

"The big legacy of the ACA may not be in access and bringing patients into the exchange," Dr. Parke said. "It may be in putting enough penalties in place to move people away from the traditional fee-for-service model."

Another change from health care reform is the growth in number of patients covered by high deductible plans through the health care exchange. In 2005, fewer than 1% of plans were high deductible plans; in 2013, that number grew to greater than 20%, and due to the exchange is expected to grow even further, Dr. Parke said. What is not widely



publicized, he said, is that a family of 4 in the United States may incur out of pocket costs of over 27% of total family income. Furthermore, many newly insured patients are not familiar with the minutia of coverage options, and so may not understand copays, deductibles, and other aspects of health plans.

"In other words, we have patients coming into our offices who have never had coverage before and don't understand how their coverage works. Many on our own staff may not understand the variables in these new coverage plans, and so, we have a tremendous challenge on our hands as to how to continue to provide excellent care," he said.

However, Dr. Parke noted, many of these consequences may not, in fact, be unintended, because 1 underlying principle of health care reform is an attempt to aggregate health care systems and to move health delivery away from the small private practice model. But because ophthalmologists do not have a lot of collateral revenue streams, only about 1% of ophthalmologists are employed by hospitals outside of academia compared to about 35% of cardiologists.

Management Options for Vitreomacular Adhesion

Harry W. Flynn Jr, MD

Despite recent advances in the management of patients with vitreomacular adhesion (VMA), a still incomplete understanding about the natural history of the disease means there is still a lack of consensus in the best approach to these patients, according to Harry Flynn Jr, MD.

Dr. Flynn reviewed the options available to retina specialists for the management of patients with VMA. Surgery is a common management strategy in VMA and/or vitreomacular traction (VMT). Studies have suggested a high anatomical success rate after surgery, but there is a risk of complications, up to and including the development of a full thickness macular hole. Dr. Flynn mentioned some words of caution that he relays to surgical fellows under his tutelage: "We operate on patients; we do not operate on OCTs."

Nonsurgical vitreolysis is an emerging concept in the management of VMA. Although pharmacologic agents are becoming popular for this indication, several studies have suggested a role for pneumatic vitreolysis—for instance, using C3F8 gas. According to Dr. Flynn, the gas bubble "may serve as a cushion for a more innocuous VMT."

Pharmacologic vitreolysis is a more recent concept, and although the "benefits are clear because it offers a nonsurgical approach, we worry about the adverse events," Dr. Flynn said. Enzymatic cleavage of intraretinal laminen may affect photoreceptor viability. "There may be some intraretinal effect of ocriplasmin [Jetrea, Thrombogenics] that may be deleterious in the long run," he said.

Studies have indicated that a large number of patients-

perhaps as many as 85%—have resolution with no intervention, suggesting a role for observation. Parsing out which patients will benefit from this is difficult, however.

"For patients who present with good visual acuity and minimal changes in terms of the size of the hole and persistent traction, an option is certainly observation," Dr. Flynn said. "Consider observational management for eyes with better visual acuity or patients who have confounding, complicating, or compounding systemic diseases."

High Myopia: What We Peel and What We Should Peel

Ramin Tadayoni, MD, PhD

Eyes with elongated axial length (ie, high myopia) may be more prone to retinal traction, and thus, peeling of abnormal membranous intraocular structures should theoretically be of benefit, said Ramin Tadayoni, MD, PhD.

Dr. Tadayoni reviewed current thinking on the 3 essential structures that can be peeled intraoperatively—an epiretinal membrane (ERM), the vitreous (hyaloid), and the internal limiting membrane (ILM)—and whether there is any benefit to this particular surgical step.

Whether to peel an ERM is a straightforward consideration, Dr. Tadayoni said: "This should not be there, so if you find it, peel it." However, whether to peel the vitreous in patients with high myopia is a more calculated decision. According to Dr. Tadayoni, it is widely believed that eyes with high myopia should be expected to have posterior vitreous detachment (PVD) on a fairly consistent basis—perhaps in 80% to 90% of cases. But in a retrospective review of patients in his clinic, Dr. Tadayoni said that intraoperatively he noted only a 50% posterior vitreous separation rate among patients with high myopia, with significant differences in separation rates related to the surgical indication. Among eyes with high myopia being operated for a macular hole or foveal schisis, 90% of eyes had an attached vitreous requiring dissection; only 25% of eyes with an ERM had attachment, a rate similar to emmetropic eyes. The result suggested that PVD may be overestimated during clinical examination, Dr. Tadavoni said

"In diseases like macular hole or foveal schisis, we should really try to find the vitreous, because in most of these cases, the vitreous is usually attached," he said. "But in ERM or retinal detachment, in most cases, you should expect that the vitreous is already detached."

Whether to peel the ILM is also discretionary. "If you have a retinal detachment, there is little rationale to peel the ILM in high myopic patients; on the other hand, if you have a macular hole, there is a strong rationale," Dr. Tadayoni said.

Whether to peel the ILM in eyes with myopic foveal schisis present an interesting challenge, Dr. Tadayoni said, as peeling the hyaloid alone could be enough in many cases.

Yet, there is a risk of creating a macular hole and/or altering the function of an already altered retina by decreasing the sensitivity to light. Dr. Tadayoni said he does not have a conclusion on whether there is definitive benefit to peeling the ILM in highly myopic eyes.

MIVS Vitreoretinal Techniques for Diabetic Detachments

Maria H. Berrocal, MD

Advances in vitrectomy instrumentation technology allow surgeons greater control for finite maneuvers during delicate operations, which is particularly advantageous in eyes of diabetic patients, said Maria H. Berrocal, MD.

Similar to cataract surgery, which has witnessed a move to smaller gauge instrumentation and minimally invasive incisions, thus reducing the risk of iatrogenic complications and surgically induced astigmatism, the advent of MIVS techniques has afforded retinal surgeons greater control in the small environment of the posterior segment, thereby reducing the risk of inducing retinal detachments and/or sclerotomy associated complications.

"A lot of people think that smaller gauge is for simpler cases, but I think this misses the point," Dr. Berrocal said. "The real advantage is in the complicated cases, because there are benefits to using these very delicate instruments in the smaller ocular environment."

Another advantage of the move to smaller instruments with vitrectomy machines capable of higher cutting rates and advanced fluidic control is that they have allowed surgeons to invent new surgical techniques and approaches, according to Dr. Berrocal. For instance, she said, she uses a 25- or



"We're not using the suction to try and lift and peel; you just lift it a little bit to create space and then you cut, and then repeat the maneuver as needed—you can do this in a fairly safe and fast manner," Dr. Berrocal said.

Dr. Berrocal said she prefers to use the maximum cutting rate available with maximum aspiration, where aspiration is then controlled via the foot pedal. Using such settings with 27-gauge instruments allows for removal the hyaloid from the retina in a very controlled manner—with the probe acting "almost like an eraser" over fibrovascular tissue, she said.

Taylor Smith Lecture: Nothing in Vein: The Evolving Management of Retina Venous Occlusive Disease

Julia A. Haller, MD

The approach and sophistication of managing patients with retina venous occlusive disorders has evolved tremendously over the past decade, Julia A. Haller, MD, said during the Taylor Smith Lecture.

Not long ago, the prevailing wisdom with venous occlusive disorders was that delaying treatment was not deleterious, that many patients' disease was self-limiting, and, therefore, that continued treatment would eventually yield a positive outcome. As well, Dr. Haller said, it was commonly thought that eyes with bad perfusion (ie, advanced disease) were too far gone to ever recover acceptable vision.

Around 2009, however, the "pharmacologic era" of treating venous occlusive disorders—branch and central venous occlusion (BRVO and CRVO, respectively)—began with a series of seminal clinical trials.

"The studies that have dramatically raised our level of sophistication about patients with retinal venous occlusion include the SCORE study, which investigated triamcinolone versus laser; the Ozurdex study, which looked at the dexamethasone implant [Allergan] in BRVO; the BRAVO and CRUISE studies that studied ranibizumab in BRVO and CRVO; and COPERNICUS and GENEVA, and now the VIBRANT study, which looked at aflibercept for BRVO," Dr. Haller said.

The anti-VEGF studies also revealed a new appreciation that delayed treatment, although effective in achieving an anatomic response, may not yield vision improvements.



One of the remaining challenges

in managing BRVO and CRVO patients is identifying who might do better without treatment. "We know some people can be followed and will do better on their own, but the real challenge is in identifying who those patients are, and right now we don't know who they are," Dr. Haller said.

In fact, the new pharmacologic age of treating BRVO and CRVO has introduced a new complexity, in that it is unknown what is the best treatment for front line therapy, which should be kept in reserve for rescue therapy, which are less effective in treatment-naïve patients, and which are most effective in recalcitrant disease. As well, Dr. Haller said, because all the therapeutic modalities treat the secondary consequence of the disease (ie, the edema), there are not curative options to offer patients.

