



ANA/NJ Newsletter

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***Acoustic Neuroma Association
of New Jersey***

A Non-Profit Corporation

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CyberKnife

A Major Advance in Gene Therapy

Congratulations to Dr. Maria Jasin, winner in 2019 of the prestigious Shaw Prize in Life Science and Medicine (the ‘Nobel of the East’) given to scientists whose research has greatly benefited humanity. Dr. Jasin is a molecular biologist at the Sloan Kettering Institute in New York City and Professor at the Graduate School of Medical Sciences, Cornell University.



Dr. Maria Jasin

As reported in the Spring 2020 issue of the *MSK News*: “Dr. Jasin began conducting her pioneering research in the 1990s. Her work eventually led to today’s cutting-edge tools for genome editing. With these methods of molecular cut and paste, scientists can make precise changes to genes, the units of heredity that specify what color your eyes are, if you’ll be tall or short, and even whether or not you have a predisposition to cancer. Genome-editing techniques offer the potential to cure people who have diseases due to inherited or acquired genetic changes.”

MSK notes: “The preferred tool of this revolution is called CRISPR/Cas9, and its development has been attributed to many investigators around the world. . . Scientists have used CRISPR to fix the genetic mistake that leads to sickle cell anemia, an inherited condition that causes blood clots and intense pain. But the origin of this technological advance relies upon a crucial discovery made by Dr. Jasin in 1994 when she showed how double-strand breaks in a DNA stimulate recombination in mammalian cells. She found a way to introduce a double-strand break at a specific spot in a mouse chromosome. The cell would repair the break but introduce mutations at the spot. But when she supplied the chromosome with an extra piece of DNA at the same time as making the break, the cell would use this new piece of DNA to complete the repair. Like a cinematographer editing a reel of film, Dr. Jasin could splice in an entirely new scene into the movie. It was the first example of what would be called genome editing.” Today’s targeted medicines are also based on knowledge gained from Dr. Jasin’s important work.¹



¹ See “The Big Break: Maria Jasin and the Discovery that Launched Gene Editing,” *MSK News* (Spring, 2020); “CRISPR Technology for Genome Editing,” ANA/NJ Newsletter (April, 2015). A video of Dr. Jasin’s Shaw Prize lecture in Hong Kong (Sept 26, 2019) can be viewed online at www.ShawPrize.org.

Notices

- The “Osia” by Cochlear is a new type bone conduction hearing system with a slim, wireless magnet-held sound processor and redesigned implant that requires no through-the-skin abutment. It’s made to work with iPhone technology. The hearing device has many attractive new features, although Cochlear advises that the Osia is not intended to replace its proven Baha system: “For some patients a Baha System may potentially be a better solution than an Osia System. Please, consult with a Hearing Implant Specialist to determine the best path forward for your individual needs.” (Cochlear.com)



- An optimistic forecast: “We are learning more about the genetics of this disease and the molecular features of these tumors. In 10 years, it’s possible we will be able to inhibit the growth of acoustic neuromas biologically, and avoid surgery.”(Mayo Clinic “Sponsor Spotlight,” ANA *Notes* (Mar 2020). The culprit NF2 gene for acoustic neuroma was identified in 1993.

- The culprit CFTR gene for cystic fibrosis lung disease was identified in 1989. For the exciting story of the 30-year research effort that led in 2019 to the drug Trikafta (effective for 90% of patients 12 years or older), see the article in the *Washington Post* and *Newark Star Ledger* (May 7, 2020), “Through Successes, Many Still Looking for Treatment,” by science writer Carolyn Y. Johnson. The author notes how “10% of cystic fibrosis patients, or about 3,000 people in the United States, are still waiting for a therapy that works for them.” (The article is also available on the Facebook page of the Cystic Fibrosis Foundation, post for April 20, 2020.)

Deciding Between Treatment Options

The Acoustic Neuroma Association (ANA) and University of California/Irvine researchers have reported on the results of an online survey of ANA members aimed at gaining a better understanding of “the critical decision-making process patients use in choosing surgery, radiation, or observation.”² A total of 789 acoustic neuroma (VS) patients completed the survey.

The survey showed:



- 474 patients (60%) cited physician recommendation as a significant influential factor in deciding treatment. A total of 32 (4%) stated the physician alone made the decision for treatment, and 29 (4%) felt they did not understand all possible treatment options before the final decision was made. Of the 414 patients who underwent surgery, 66 (16%) felt they were pressured by the surgeon to choose a surgical treatment.

² See Hamid Djalilian et al, “Patient Decision Making in Vestibular Schwannoma: A Survey of the Acoustic Neuroma Association,” *Otolaryngol Head Neck Surg*, vol 158 (May 2018); Hamid Djalilian, “Patient Decision-Making in Vestibular Schwannoma,” ANA *NOTES* (June 2019).

- 629 patients (80%) saw multiple VS specialists, and 410 (52%) sought second opinions within the same specialty. Of those who received multiple consults, 242 (59%) reported receiving different opinions regarding treatment.
- Patients who chose observation spent significantly less time with the physician (41 min.) compared to surgery (68 min.) and radiation (60 min.).
- “Deciding on a proper treatment for VS can be complicated and dependent on numerous clinical and individual factors. Our findings demonstrate that those who seek second opinions have higher satisfaction rates. Physicians should facilitate and help patients seek second opinions to better understand the various treatment modalities that can be offered.”

A Mayo Clinic study has asked if simple geography, where you live, could influence treatment selection for VS.³ The researchers used a database called SEER (Surveillance, Epidemiology, and End Results) that identified 9,761 patients with VS across 16 geographic registry areas. A strong association between place of residence and treatment modality for tumors up to 3 cm in size was found. “In many cases, the impact of place of residence on treatment selection was greater than other established variables such as tumor size and age.” The data suggested that treatment selection was being significantly influenced by regional referral patterns, provider or institutional treatment preferences, and regional availability of subspecialty expertise. “Despite a lack of compelling evidence supporting one treatment modality over others, many providers and institutions remain highly biased toward one particular therapy – microsurgery, radiation, or primary observation.”

The study concluded: “Understanding geographic bias is important for patients, referring physicians, and treatment providers alike. Until there is clear evidence supporting one therapy over others, multidisciplinary consultation, with a minimum of a neurotologist, neurosurgeon, and radiation oncologist or radiosurgeon, should be offered in order to provide balanced counseling and accurate informed consent.”

Comparing Radiation Treatments: SRS vs. FSRT

Acoustic neuroma patients ask how radiation treatment outcomes compare between single-fraction radiosurgery (SRS) and multiple-fraction radiotherapy (FSRT).

Section No.7 of the “Guidelines on the Management of VS” compiled by the Congress of Neurological Surgeons (2018) is one place to go for answers to this question.⁴ Another study to look at is the joint report published in 2017 by researchers in departments of neurosurgery in Sweden, Norway, Denmark and Israel.⁵ It’s noteworthy that this report complains of “a lack of high-quality studies comparing radiation therapy alternatives for patients with VS.” No randomized controlled studies comparing SRS and FSRT were found. Dr. Morten Lund-Johansen (Bergen, Norway) observed: “Nearly all reports are ‘single treatment, single center,’ and very few high-quality comparative studies exist. It is a difficult challenge for the neurosurgical community to conduct multicenter comparative studies on VS.”

³ M.L. Carlson et al, “Does Where You Live Influence how Your Vestibular Schwannoma is Managed? Examining Geographical Differences in VS Treatment across the U.S.,” *Jour Neurooncol*, Vol 129(2) (Sept 2016).

⁴ See ANA/NJ Newsletter (October 2018).

⁵ O.Persson, J.Bartek et al, “Stereotactic Radiosurgery vs. Fractionated Radiotherapy for Tumor Control in VS Patients: A Systematic Review,” *Acta Neurochirurgica (Wien)*, vol 159(6) (April 2017). Both abstract and free full-text copy available at PubMed.gov.

These investigators screened 1,094 studies for the period 1995-2014. To be included in their report, studies needed especially to involve a minimum of 50 adult patients (>18 years); show long-term follow-up of 5 years or more; and indicate any interventions required after the initial treatment of the tumor. Only 19 studies were found to fulfill all inclusion criteria. Of these, 17 reported outcome data for SRS, and only 2 for FSRT. The number of patients reported on was 2,834 for SRS and 356 for FSRT.⁶

What was concluded from this systematic review of the medical literature?

Tumor control. “The current data provides no indication of one treatment technique being superior to the other with reference to tumor control.” The tumor control rate was 92-100% for both treatment options. “Loss of tumor control necessitating a new VS-targeted intervention was found in an average of 5.0% of patients treated with SRS and in 4.8% treated with FSRT.”

The need for more FSRT case studies was emphasized. One study was identified reporting on hypofractionated radiotherapy (HfRT) for VS using the CyberKnife (that is, 18 Gy in 3 fractions).⁷ This study showed “a favorable outcome with no need for reintervention in any of the 117 treated patients within the 61-month median follow-up. [However], since HfRT from a radiobiological point of view is likely to be more similar to SRS than to FSRT, this study was not included in the FSRT group.”

Facial and trigeminal nerves. The risk of deterioration for these nerves was less for SRS compared to FSRT. “The risk for facial nerve deterioration was 3.6% for SRS and 11.2% for FSRT, and for trigeminal nerve deterioration [the risk was] 6% for SRS and 8.4% for FSRT.”

Hearing preservation. The chance of preserving hearing showed no difference between the two groups. “The mean deterioration ratio for patients with serviceable hearing before treatment was 49% for SRS and 45% for FSRT, respectively.”

Controlling Post-Surgery Headache

by Brad Zimmerman*

I had retrosigmoid surgery for a large acoustic neuroma in May 2010. My headaches didn't begin until about 30 days after my surgery. Although now infrequent, I still get them today, ten years later. The pain radiates from the surgery site at the skull base and down through the neck muscles into the shoulder area. The best comparison I can give is that it feels like an extremely bad, continuous muscle cramp in my head and neck. For the first two to three years after my surgery, I had constant, chronic discomfort. At its worst, the pain was severe and debilitating to the point I had to remain in bed. At its best, it was a nagging aggravation, but I was able to function normally for the most part. Luckily, as my doctor reassured me, the headaches came less frequently as time went on.

⁶ Tumor sizes were less than 3 cm. All SRS studies had median marginal dose of 12-13 Gy. FSRT had median total dose of 50 Gy in fractions of 1.8-2.0 Gy.

⁷ J.T.Tsai et al ,”Clinical Evaluation of CyberKnife in the Treatment of Vestibular Schwannomas,” *Biomed Res Int* (2013), Free full text available at PubMed. Tumor control was excellent at 99.1%; hearing preservation rate was about normal for VS. “With a follow-up of 64.5 months, 12 patients who had poor hearing before treatment (Gardner-Robertson II) experienced hearing degradation; they appeared to have larger tumor sizes, smaller cochlear sizes, and higher prescribed cochlear doses compared to the patients with preserved hearing.”

* Brad Zimmerman is listed in the March 2020 ANA/NJ Directory. He invites questions and discussion.

After speaking to my surgeon and a number of physicians, and experimenting with different treatments, I came up with some options that worked for me. They didn't totally relieve the discomfort or occurrence of the headaches, but they controlled them to a point I could work and lead a relatively normal lifestyle. I'd like to emphasize that self-medicating and experimentation with pain management without consulting your physician can lead to dangerous consequences. Even taking over-the-counter pain medications on a regular, long-term basis can have potentially dangerous and negative side effects. You certainly have to try different options to see what works for you, but only after gaining the approval and input from your doctor. I've attempted to be as accurate as possible in this article, but I'm not a doctor nor do I possess any expertise in this area other than my own experiences, so the opinions are my own.

Since I dislike opioid medications, I made no attempt to factor them into my treatment plan. I wanted to develop a safe and responsible schedule for using over-the-counter, non-prescription NSAID's to control my pain. But there are potential dangers using these medications on a daily basis. One problem is that long-term daily use may cause rebound headaches, which can exacerbate your current pain and lead to a cycle of dependence. Also, products containing caffeine, which is a common ingredient in migraine pain relievers, have a higher tendency to cause rebound headaches. And acetaminophen can potentially cause liver damage if recommended dosages are exceeded. These products are also inherently blood thinners, and can cause other medical issues with long-term use. So as I've stated, you need have a discussion with your doctor before starting any type of NSAID regimen to avoid these complications.

I found that migraine relief products that contain acetaminophen, aspirin, and caffeine worked the best. A close second was ibuprofen products. I personally received little benefit from naproxen, so I didn't factor it into my regimen. To lessen the negative side effects I discussed, I alternated use of the migraine aspirin and ibuprofen. Generally speaking, the manufacturers state on their bottles that you can take two of these pain relievers every four hours, not to exceed eight pills in a twenty-four hour period. Knowing my headaches might require long-term use, I wanted to take as little medication as possible to maintain functionality. I found that taking one pill in the morning, then one approximately every four hours for a total of four pills daily took the edge off my discomfort and worked well. I would consume one migraine aspirin, then four hours later one ibuprofen, and would continue that rotation. This allowed a reserve of four extra pills in a twenty-four hour period in case I might experience an extremely severe or long duration headache. Using this regimen even if I had to take the additional four pills, I would not exceed the recommended daily dosage by the manufacturers and could maintain a constant level of pain reliever in my system. My physician felt that this was a safe plan that could be utilized long-term without being detrimental to the body. To avoid stomach problems, I took over-the-counter omeprazole on the recommendation of my doctor. I also had blood tests done during my annual exams to ensure there were no medical complications taking place since I was taking these medications on a regular basis.

Eventually as the headaches lessen over time, you want to have a plan to discontinue their use. I definitely experienced rebound headaches when I suddenly cut back, so I came up with a plan of eliminating one pill from my daily regimen as my pain would allow. Taking the reduction over time, it seemed to lessen the rebound headache problem. Once I could get away with eliminating one pill, I'd start eliminating a second pill. If need be, I would eliminate the pill every other day until I could stop it totally. Another method is to cut the pill in half and take a half dose if the type of pill taken would allow for it. This way you can cut back an even smaller dose at a time, lessening the negative effects even more. I had times when I had to take a few extra pills here and there, but eventually as the occurrence of headaches subsided over time, I was able to get off the pain medication totally and only take it when a sporadic headache occurred.

I want to mention that in addition to medication as the main component of my pain management plan, I also used acupuncture performed by a physician to lessen my discomfort and found it to be valuable. Keeping calm and stress-free assists in eliminating tensions that exacerbate headaches. I tried to stay as totally relaxed as possible, learned to better manage stressful situations and incorporated a stretching routine

into my daily activities. Aerobic exercise was also very helpful to me. During bouts when the pain became debilitating, I found that trying to fight through it was not only impossible but also non-productive. I just took a nap and stayed in bed until it subsided sufficiently to resume activities. Chronic pain is fatiguing. A good diet, staying well hydrated and getting proper sleep are all very important. I'd like to mention that chronic pain over long periods of time can cause you to be edgy, anti-social and quite impatient at times. Since other people, especially your loved ones and work associates, are not mind readers, nor feel your discomfort, it's important to tell them what you are experiencing and how it effecting you so they understand your mood and personality changes. I found that keeping silent in the belief that you don't want to be a "constant complainer" only complicates issues. The pain is very real. You don't want to whine, but you definitely want to make people aware of your issues so there are no misunderstandings.

Finally, my doctor warned me that feelings of depression are common after this type of surgery and with these chronic headaches. Being armed with that knowledge, when these negative emotions presented themselves, I acknowledged them as existing, but refused to let negative feelings take root. I knew for a fact that they were part of the recovery process, and I just ignored them. This was very effective for me. I know that many people may be critical of my solution, but I mention it only as my way of dealing with the problem. It's important that you find your personal solution as everyone is different. Don't be afraid to talk to a loved one, your pastor or a doctor about depression and methods to deal with it. Find what works for you. I wish you all the best in your recovery. We are all in this together. There is definitely light at the end of the tunnel!

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Notice: ANA/NJ Group Meetings are on Hold!



The members of the Executive Board regret that our usual October 2020 AN support group meeting cannot be scheduled at this time due to COVID-19. This has been distressing since bringing acoustic neuroma patients, family and friends together for mutual support and to share experiences and information has been a main purpose of our association since its founding in 1995. A special notice will be sent to members and posted on the website and our Facebook page as soon as a next meeting can be scheduled.

We are aware of the new 'virtual meetings' technology (Zoom, Skype, Webex) that can bring people together who have smart phones and computers equipped with a mic and camera. It's under discussion and we may give it a try. Stay tuned.

Meantime, we have used the current ‘time-out’ to redo and update our ANA/NJ website, www.ananj.org. Take a look. Your appraisal and/or any recommendations you would like to make will be welcomed. Phone or email Wilma Ruskin (609-510-9039; wruskin33@aol.com).

Facebook is another way for AN patients to be in touch during this period of ‘social-distancing.’ Our Facebook page (Acoustic Neuroma Association of NJ) is active and doing well, but could benefit from broader participation. People use Facebook looking for information and asking for advice.

Wilma continues to receive phone calls from new AN patients asking for assistance. Our revised website link, info@ananj.org, should also be working soon for sending inquiries directly to Wilma. A copy of the latest ANA/NJ Directory (March 2020) is sent to new patients so that they can get in touch with patients willing to share their personal experiences with acoustic neuroma – e.g., symptoms, treatment, postop issues, medical providers, hearing aids.

We still believe that being able to meet and talk face to face with other patients is very important for the newly diagnosed ANer. But in the meantime, there are these other ways we can be of help.

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