The ANA/NJ Mini-Conference
October 26, 2014

October 26 may have marked the 2nd anniversary of hurricane 'Sandy', but by all accounts ANA/NJ's Mini-Conference at Berkeley Heights was still a great success. There were fifty-one registrants and an unprecedented nine speakers. Suzanne Milani, the meetings coordinator for Summit Medical Group, had the rooms ready for us. A representative of Cochlear Americas, Kim Blanch, was present for demonstrations of the BAHA. One attendee drove all the way from Ithaca, NY, to be at the meeting. There were people from Maryland and Delaware. The box lunch was actually pretty good. And there were lots of good people to meet and share experiences.

Dave Belonger, our vice president for ANA/NJ, welcomed everyone, and began the meeting by saying some very kind words about the organization and the volunteers who keep it running. The positive audience response was appreciated. Dave then introduced Dr. James Liu (NJMS/Rutgers), moderator of the morning Doctors' Panel for the topic "Diagnosis Acoustic Neuroma: What Next?" Dr. Liu explained that the panelists, himself included, would be looking (on screen) at MRI images of representative cases

of "The Good, the Bad, and the Ugly" among acoustic neuroma. The job for the panelists would be to discuss and decide upon best treatment(s) for each case. As shown in the photo (from left to right) the three other panelists were Dr. Michael Sisti (NY-Presbyterian),Dr.Christopher Farrell (Thomas Jefferson Univ) and Dr. Philip Stieg (Weill Cornell).

The first MRI was said to be an example of the 'Good' – a young male patient, age 38, who presented with a quite small tumor, mild hearing loss, vertigo, and some tinnitus. Summarized, the panelists' responses were: (1) Dr. Sisti – use Gamma Knife, low dose (11 Gy); (2) Dr. Stieg –Wait-and-Scan; (3) Dr. Farrell – treat the tumor if hearing preservation is a main concern for the patient, but want to learn more about the vertigo. Dr. Liu informed the panelists that this patient underwent retrosigmoid surgery (RS): the tumor "shelled out nicely," he said. With regard to the RS surgery, Dr. Liu used slides to illustrate a new procedure for fat graft-assisted cranioplasty to avoid potential problems with postoperative CFS leaks and headaches.[1]

[1] James Liu, Robert Jyung et al, "Reconstruction after Retrosigmoid Approaches . . .,"*Acta Neurochirurgica* (August 2014).

A second MRI, to represent the case of a 'Bad' acoustic neuroma, was of a 62-year old woman, moderate-sized tumor, hearing loss in the affected ear, plus ataxia (a walking problem). Briefly: (1) Dr. Farrell --"take it out," but he would like to learn more about the ataxia; (2) Dr. Stieg -- the same, use either RS or translabyrinthine (TL) surgery, although prefer RS because of shorter operation time; (3)Dr.Sisti -- RS surgery recommended. Dr.Liu revealed that eventually the decision for this patient was RS surgery.

Finally, for the 'Ugly,' an MRI for the really giant tumor of a 40-year old woman was shown. Dr.Farrell took one look and declared it "a project." The panelists immediately ruled out any initial radiation treatment. Hearing was already lost, but saving facial nerves remained a challenge. It would have to be a partial removal by surgery, probably in two stages. How much tumor could be left behind? These were matters discussed at some length by the panelists.

The rapid flow of ideas among experienced neurosurgeons during these evaluations of MRIs was fascinating and instructive. Did you see the little tail of the small tumor reaching out toward the cochlea in that one MRI? It was instructive to have the panelists point this out for us and discuss its significance. As the old saying goes, "One sees only what one knows."

Following a good lunch, the afternoon began with a Keynote Address – "Genomics, Personalized Medicine and Acoustic Neuroma," delivered by Dr. Matthias A. Karajannis, a dedicated researcher at NYU Langone Medical Center who combines genomic/molecular science with clinical trials in search of therapeutic drugs capable of helping control growth and hearing loss in acoustic neuromas, both familial (NF2) and sporadic. His talk was impressively scholarly with numerous charts, tables and references. He reported that clinical trials thus far with carefully selected existing drugs (e.g.,lapatinib) have shown some success. Encouraging improvements in hearing, as well as cases of tumor shrinkage, have been recorded.[2] Other drug studies (e.g, everolimus) are underway. And combination drug therapies may need to be tried. There may also be the need to develop and test a new generation of drugs designed for acoustic neuroma. For NF2 patients with bilateral tumors, as well as Wait-and-Watch patients with sporadic tumors seeking to avoid or delay treatment, a tumor suppressor oral medication will be very much worth all efforts.[3]

Genomic analysis in support of targeted therapies is a growing part of medicine today. The Rutgers Cancer Institute of NJ, for example, just received a $10 million anonymous grant "to help its scientists discover targeted therapies for hard-to-treat cancers."[4] Acoustic neuroma is not a cancer, but research in any one area of "precision [personalized] medicine" ultimately benefits all others.

The afternoon Doctors' Panel, moderated excellently by Dr. Samuel Selesnick (Weill Cornell), was an examination of "Treatment Modalities & Hearing Preservation Outcomes" with focus on the various types of radiation treatment available to acoustic neuroma patients.

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[2] M.Karajannis et al, "Phase II Trial of Lapatinib in Adult and Pediatric Patients with Neurofibromatosis Type 2 and Progressive Vestibular Schwannomas," *Neuro Oncology*, vol.14(9) (Sept 2012).

[3] For those not present at the conference, a good impression of the complexity of research in the field (and its unique vocabulary) can be had by looking at Dr. Karajannis' journal article dealing with 'Merlin', the tumor suppressor protein encoded by the NF2 gene. Go to www.pubmed.org and search for "Merlin: a Tumor Suppressor with Functions at the Cell Cortex and in the Nucleus," *EMBO Reports* (March 2012), free full text.

[4] Newark *Star-Ledger* (October 9, 2014)

(From left to right: Drs. Selesnick, Farrell, Danish, Schwartz and Tsai)

Dr. Shabbar Danish (RWJ) reported first on single-session radiosurgery using the most recent model Gamma Knife called 'Perfexion'. Compared to the earlier Model C (1999), the Perfexion (2006) has cut treatment time from 80 to 30 min; setup takes 3 sec rather than 10 min; and there is automatic, time-saving patient repositioning. Low dosages of 12.5-13 Gy at the tumor margin have resulted in improved rates of hearing preservation. Dr. Christopher Farrell (Thomas Jefferson Univ) pointed out how experiences with radiation treatment near the optic nerve have demonstrated the value of delivering radiation in a series of small doses or 'fractions' (radiotherapy) rather than in a single-session (radiosurgery). Along with the other panelists, he advocated dose 'fractionation' for patients most anxious to preserve useful hearing. At Jefferson, the dedicated NovalisTX linac (Varian) has been used for fractionation treatments of 5 weeks, 25 sessions. Dr. Louis Schwartz at Overlook Hospital prefers the CyberKnife linac (Accuray) for 5 daily sessions of 30 min each. Dr. Henry Tsai reported that Proton Beam treatments at the ProCure Center in Somerset are typically 25-30 sessions over 5 weeks.

The panelists agreed that small tumors do best for hearing preservation, and that tumor location away from the cochlea, as well as keeping any radiation dose to the cochlea as low as possible, are extremely important for hearing preservation. Also, as studies of Wait-and-Scan in Denmark have shown, acoustic neuroma patients who start with good hearing are the ones who end up with the best hearing.[5]

The panelists pretty much stayed away from citing and/or comparing long-term outcomes for the various types of radiation treatment. Actually, long-term data, like rates of service-able hearing at 1, 3, 5, 7 and 10 years following treatment, is only just beginning to appear. Most reports by treating centers are for 3 or 5 years at most, and hearing rates are usually not well defined. Follow-up audiometry by patients is hard to get. And then, too, radiation technology/precision has been improving so rapidly: Gamma Knife is now in its 4th version since introduction in the US in 1987; Varian has just (2010) brought out a "next-generation," "super" linear accelerator named TrueBeam.[6]

Dr. Farrell did recommend attention to one study of long-term outcomes that reminds us the effects of radiation take time to develop.[7] In this study, median audiometric follow-up was 9.3 years for 44 radiosurgery patients treated by 12-13Gy, 1997-2002. The average rate of serviceable hearing following treatment was 80% after 1 year, 55% after 5 years, and 23% after 10. Important variables used to predict outcomes were tumor size and preoperative hearing capacity. The study advised "these data demonstrate the importance of long-term follow-up when reporting audiometric outcomes. . . ."

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[5] See ANA/NJ Newslettter, April 2011 & Sept 2014.

[6] See www.variantruebeam.com/press.

[7] B.Pollock et al, "Long-term Hearing Outcomes following Stereotactic Radiosurgery . . . ," *Journal of Neurosurgery*, vol.118 (March 2013). Mayo Clinic.