

NEUROtransmitter

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Understanding the Non-Motor Symptoms of Parkinson's Disease

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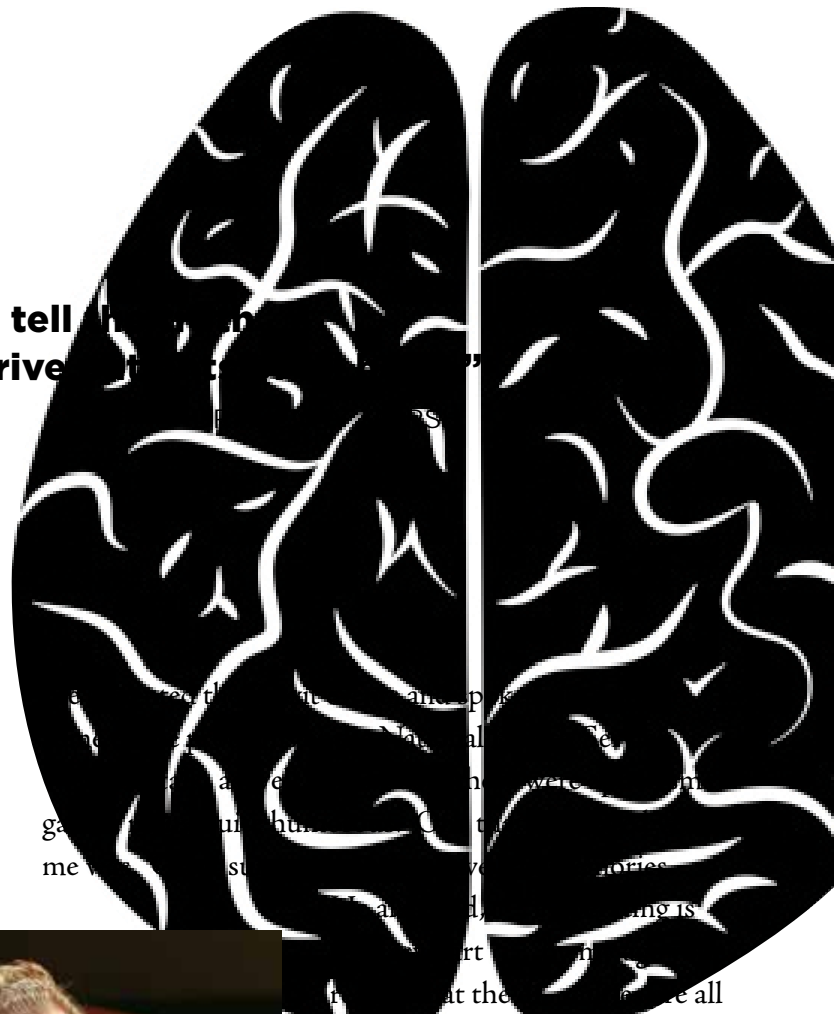
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**9th Annual
Saving the Brain
Symposium:
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Cottage
Health

“Surgeons must always tell the truth but rarely, if ever, deprive patients of all hope.”



Dear Colleagues,

Primum non nocere, translated from Latin to English, means Do no harm, a central tenet of the Hippocratic Oath to which every medical student pledges their allegiance. This phrase is also the title of a 2014 best seller by recently retired British neurosurgeon, Dr. Henry Marsh. Until 2015 Dr. Marsh was the senior consultant neurosurgeon at the Atkinson Morley Wing of the St. Georges Hospital in London and was widely reputed to be one of the most accomplished brain surgeons in the UK. He has also been recognized for his decades of work with neurosurgeons in the Ukraine and was the subject of two BBC documentaries, in 2003 and 2009.



THOMAS H. JONES, MD

We were honored to welcome Dr. Marsh as the 2016 keynote speaker for our 9th annual *Saving the Brain* Conference. He flew to Santa Barbara from medical missionary work in Kathmandu and, to underscore his resiliency, ran several miles soon after landing. Dr. Marsh's talk was entitled, Brain surgery is difficult (but not for the reasons you think). He spoke about the importance of recognizing commonplace cognitive biases during patient care and surgical decision making. In a very self-acing way, he presented surgical cases in which he had erred and from which important lessons were learned. He spent some time talking about his close relationships with American neurosurgeons, even helping with their residency training.

to do with the decision making. Another statement that attracted my attention was from his book, and concluded, Surgeons must always tell the truth but rarely, if ever, deprive patients of all hope. Importantly, he went on to add, life without hope is hopelessly difficult but at the end hope can so easily make fools of us all.

Dr. Delio, in an article beginning on page 6 of this issue of *NEUROtransmitter*, nicely summarizes the entire symposium. By all criteria it was the most successful, engaging and well attended thus far. Dr. Marsh led the day and engaged the audience, and I would encourage all our readers to purchase a copy of his book.

Sincerely,

THOMAS H. JONES, MD
Neurosurgeon and Medical Director
Santa Barbara Neuroscience Institute at Cottage Health

Robotic Exoskeleton Holds Promise for Patients with Severe Neurologic Injury

BY NOAH GAINES DPT, NCS, Physical Therapist III, Cottage Rehabilitation Hospital

A key role for any physical therapist is training patients to walk again after a severe injury. Advances in robotics hold promise to improve these patients' outcomes.

ROBOTIC-ASSISTED gait training is not required for the less-impaired patient. For them, facilitation from a physical therapist can consist of verbal and tactile cues. However, gait training for a patient with a severe neurologic injury is often more complex. For the patient that lacks

the strength, coordination or balance to walk independently, the physical therapist must provide hands-on assistance. This can include moving the patient's limbs through swing phase, stabilizing them in stance phase, and maintaining their upright posture and balance throughout.

Of course, this requires significant physical effort and the quality and quantity of steps taken by the patient can be limited by the physical abilities of both the patient and the physical therapist.

Gait training exploits neural plasticity of the cortex and spinal cord to regain locomotor ability. While some plasticity does occur spontaneously, it is also found to be task specific and use dependent. For extremely impaired patients, robotic assistance allows the high number of quality repetitions and appropriate sensory feedback required to promote neural plasticity.

Robotic Exoskeleton at Cottage Rehabilitation Hospital

In March 2016, Cottage Rehabilitation Hospital

Cottage Rehabilitation Hospital physical therapists Noah Gaines DPT, NCS, and Amber Gonzalez, DPT, demonstrate use of the robotic exoskeleton.

acquired an Ekso wearable robotic exoskeleton, currently the only exoskeleton cleared by the FDA for use with patients after stroke and spinal cord injury. While exoskeletons were originally designed to allow a person with a complete spinal cord injury to stand and walk, we now use them as tools to help patients regain the ability to walk outside of the device.

To walk in an exoskeleton, the patient is fully strapped into the suit while battery powered motors drive the hip and knee joints. Ekso has modified its devices significantly to make them more appropriate for assisting with recovery rather than just replacing deficient muscles. To initiate stepping in the Ekso, the patient must weight shift adequately and activate a sensor. Furthermore, the Ekso can sense how much assistance the patient requires and adjusts the help that it provides accordingly. This encourages patients to increase their volitional movement.

Little Research but Compelling Studies

V. Reggie Edgerton's research demonstrates how robotic-assisted gait training in mice with spinal cord injuries is most successful when it includes variability of tasks and is "assist-as-needed." On the other hand, he found that monotonous repetition of the exact same task results in learned disuse¹. While the physical therapist will often trigger the steps for the patient during the initial training, the patient initiates their steps with weight shifts and knee flexion during the majority of the



training sessions. High repetitions of patient-initiated steps are the proposed mechanism for increased motor learning in the Ekso.

Because exoskeletons have only been made available for patient use in the last five years, there is not a robust body of research to support their use. However, there are compelling studies that show the potential that these devices hold for increasing recovery after neurologic insult. In a study in which 105 patients with spinal cord injury received robotic-assisted gait training (five days a week for eight weeks), the greatest rate of improvement was shown in the acute motor incomplete patients. At the end of their therapy, they walked faster and required less assistance than their matched peers receiving conventional therapy². In a second study, stroke survivors who performed Ekso gait

training during inpatient rehabilitation demonstrated improved functional independence measures compared with their matched counterparts³.

Conclusion

Walking is a crucial part of patients' identities and independence. It can be devastating when that ability is lost. That is why it is exciting to have a new tool to assist these patients on their journey through rehabilitation.

¹Edgerton VR, Roy RR. Robotic Training and Spinal Cord Plasticity. *Brain Res Bull*, 2009 Jan 15;78(1): 4-12.

²Benito-Penalva J, et al. Gait Training in Human Spinal Cord Injury Using Electromechanical Systems: Effect of Device Type and Patient Characteristics. *Arch Phys Med Rehabil*, 2012 March; 93(3): 404-12.

³Russo A, et al. Impact on Discharge Destination for Individuals with Acute Stroke. *Stroke*. 2016; ATP149.

For more information on the Santa Barbara Neuroscience Institute at Cottage Health, visit www.cottagehealth.org/neuro



CASE STUDY: **Exoskeleton Helps Multiple Trauma Patient Regain Mobility**

A 62-year-old man was cleaning vines from a tree and fell 30 feet. He was admitted to the Emergency Department with multiple traumas, including nondisplaced fractures of the dens of C2 and the posterior element of C5, which were stabilized with a Miami J collar. Additionally, burst fractures at L1 and L3 caused stenosis of the spinal cord and were stabilized via anterior/posterior fusion (T11 – L5). He also had multiple rib fractures, a right pneumothorax, sternal fracture, right humeral neck fracture (which was surgically repaired), and a left distal radius fracture.

Forty days after his initial injury, the patient was transferred to Cottage Rehabilitation Hospital. At that time, he required total assistance for bed mobility and transfers. With maximum assistance, he was able to stand for 10 seconds. Gait did not occur because the activity was unsafe for the patient, given his weakness. The severity of the patient's spinal cord injury was tested to be an ASIA Impairment Scale C2 D (motor incomplete). This gave him an excellent prognosis to return to walking. The patient worked with

physical therapy, occupational therapy, speech language pathology, and therapeutic recreation for five to six hours per day and improved his strength and endurance but was still unsafe to walk.

Sixty-one days after his initial injury, he took his first steps since his injury in the Ekso with two therapists assisting him for balance and weight shifting. He reported that walking in the robot gave him confidence and made walking seem like a reality. Shortly afterwards, he began gait training short distances out of the Ekso with a bilateral platform walker. As his strength, balance and endurance improved, he progressed from using a front-wheeled walker to bilateral Lofstrand crutches.

By the time of his discharge, 79 days after his injury, he showed large gains in all areas of functional mobility. With light minimal assistance from his physical therapist, he was able to walk 377 feet in six minutes using only bilateral AFOs and a bilateral platform walker. He was also able to perform all bed mobility and transfer tasks with supervision and without assistance.

Ekso Session	1	2	3	4	5	6	7
Walk time	5:14	11:14	9:21	11:17	20:00	17:41	18:12
Up time	12:30	24:12	20:52	20:17	36:26	25:01	30:51
Total steps	111	238	228	346	366	375	409

Keynote speaker
Dr. Henry Marsh



Ninth Annual *Saving the Brain* Symposium Focused on the Latest Advances in Neuroscience Research and Treatment

BY PHILIP R. DELIO, MD, Stroke Neurologist and Medical Director of Stroke Services at Santa Barbara Cottage Hospital

THIS YEAR'S 9th annual *Saving the Brain* Symposium featured an outstanding group of guest speakers, each providing a glimpse into the latest advances in the field of neuroscience research and treatment.

As always, the insight and predictions offered by **Thomas H. Jones, MD**, Medical Director of the Santa Barbara Neuroscience Institute (SBNI) at Cottage Health, for how health care and the neurosciences will evolve in the next decade was a provocative look at how we currently practice medicine.

This was a perfect segue to the lecture by our keynote speaker, Henry Marsh, MD, CBE, FRCS, acclaimed author and neurosurgeon, who gave a presentation on what it means to be a neurosurgeon and the critical decisions made in the operating room every day. His expertise and clinical acumen seem to be only surpassed by his

humility, as he focused on how caregivers can evolve, learn and advance care to improve outcomes.

Susan Chang, MD, a professor in the Department of Neurological Surgery and Director of the Division of Neuro-Oncology at the University of California, San Francisco, gave a fascinating talk on the genomics of neuro-oncology, and how genetic markers can predict response to therapy and guide treatment choices. Her work at UCSF is setting a new standard in treating primary central nervous system malignancies, and in a disease traditionally viewed with skepticism in regards to prognosis, her work provides hope and optimism for the future of brain tumor medical management.



Mary Amatangelo, RN, from Brigham and Women's Hospital highlighted the different

Continued on page 11



Dr. Susan Chang



Dr. Grace Park,
Dr. John Park,
Lisa Moore, VP,
Clinical Services



Dr. Michel Kliot,
Dr. Henry Marsh,
Dr. Susan Chang



Dr. John Park



Left to Right:
Pam Jones, Dr. Pamela Jones,
Dr. Tom Jones, Dr. Henry Marsh,
Traci Rodriguez , Connie Boyd, RN



Understanding the Non-Motor Symptoms of Parkinson's Disease

BY ERIN PRESANT, DO, Neurologist

The non-motor symptoms of Parkinson's disease have long gone underrecognized and undertreated. Increasingly the focus of new studies, the non-motor symptoms are the primary source of decreased quality of life for patients and can be the most difficult symptoms to treat. The non-motor symptoms are not usually helped by most common Parkinson's disease medications or by surgical treatments like deep brain stimulation (DBS) that are used for motor symptoms.

PARKINSON'S affects virtually every system in the body. Non-motor symptoms are usually mediated by the non-dopaminergic pathways. These areas, as well as some of the other pathways in the brain, are a major target for new research and the development of new drugs.

Non-Motor Symptoms of Parkinson's Disease

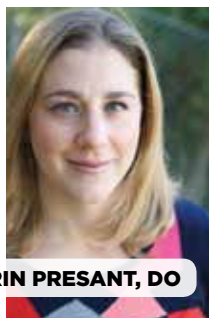
The non-motor symptoms of Parkinson's disease are wide-ranging. They can encompass anosmia, constipation, REM behavior sleep disorder, impulse control disorder, orthostatic hypotension, dementia, psychosis and hallucinations, urinary dysfunction, sleep disturbances, anxiety, depression, pain, speech disturbances and dysphagia. It is important to understand their effect on the quality of life of Parkinson's patients and to treat them appropriately.

The image highlights the motor tracts found in Parkinson's disease. Red areas along the tract show regions that are significantly different from healthy controls.

Constipation is a significant issue in Parkinson's and the gut has become a major area of research. Degeneration of neurons is seen in the myenteric plexus of the colon of Parkinson's patients, and Lewy bodies may be present in the gut as well. A recent retrospective Danish study (Svensson E et al, 2015) implicates the vagus nerve as a transport mechanism of Parkinson's from the gut to the brain. The early and complete severing of the vagus nerve reduced the incidence of Parkinson's in half as compared to the general population. Constipation can be treated conservatively with dietary changes and increased fluids. Other treatments can include stopping constipating medications, exercise and stool softeners.

Up to 75% of Parkinson's patients will experience **dementia** related to Parkinson's. Of the other 25%, at least half will experience cognitive problems associated with Parkinson's. The most common difficulties seen in Parkinson's dementia include executive functioning impairment (impaired planning and working memory); visuospatial deficits; attentional deficits; and language dysfunctions (the "tip of the tongue" phenomenon or expressive difficulties). Dementia is associated with diffuse Lewy body disease. Treatment involves the same drugs that are used to treat other dementias.

Psychosis and hallucinations can be present in Parkinson's in conjunction with other dementia symptoms. Early hallucinations are a risk factor for developing Parkinson's disease dementia. If hallucinations and cognitive problems are present before any motor symptoms, they are more likely to represent Lewy body dementia as opposed to Parkinson's disease dementia. Psychosis and hallucinations can be worsened by dopaminergic medications that are used to treat motor symptoms. Quetiapine (Seroquel), begin 12.5 mg-25 mg QHS, is



ERIN PRESANT, DO

The non-motor symptoms of Parkinson's disease are wide-ranging. It is important to understand their effect on the quality of life of Parkinson's patients and to treat them appropriately.

typically used to treat. Anecdotally, we do see improvement, but in large-scale studies it's been somewhat questionable. Typical antipsychotics, especially Haldol, should be avoided as they will worsen the patient's Parkinsonism.

Sleep disturbances are reported in about 90-95% of Parkinson's patients, making it one of the most commonly reported non-motor symptoms. Dopamine plays a role in arousal, wakefulness and sleep through the ventral tegmental area and the D2 receptors. Insomnia is a typical sleep disturbance. Sleep aids like Ambien and Lunesta should be avoided in

Parkinson's patients as they can cause abnormal behavior. Patients who do not want to take anything for sleep should be encouraged to try sleep meditation practices or mindfulness. It's important to note that dopamine agonists can also cause severe daytime sleepiness. Patients can be

asked to keep a diary to help determine whether there is a correlation between when they take their medication and their sleep disturbances.

REM sleep behavior disorder (RBD), a parasomnia characterized by the lack of muscle paralysis during REM sleep, is specific to neurodegenerative diseases. A complicated mechanism, not fully understood, may involve a dysregulation of multiple brainstem nuclei leading to the lack of atonia during REM sleep. Up to 75% of patients with RBD go on to develop Parkinson's. Clonazepam at bedtime, 0.25-0.5 mg to start, can be used to treat RBD. Melatonin (3-12 mg at night) may be a better option for an elderly population susceptible to falls, confusion or cognitive problems, either used alone or in conjunction with clonazepam.

Anxiety is frequently seen in Parkinson's. The risk factors in Parkinson's patients for developing

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Parkinson's Disease continued from page 9 anxiety disorders include being female, motor fluctuations, and a history of a previous anxiety disorder. Anxiety sometimes can be related to the wearing off of medications, so having patients keep a diary of when they are taking their medications and when their anxiety is coming on can be helpful. Avoiding long-term use of benzodiazepines due to potential side effects is best. Use of SSRI antidepressants can be helpful, as well as optimizing the levodopa therapy to reduce fluctuations. Psychotherapy, meditation, mindfulness techniques and yoga can help reduce anxiety in patients not wishing to take medications. It's important to note that motor symptoms will worsen if anxiety and depression are not well controlled.

Depression may involve multiple specific neuronal pathways that previously

weren't considered to be affected in Parkinson's disease. Because of this, we see depression at higher rates in the Parkinson's patient population than in the general population. Depression in Parkinson's patients typically is characterized by apathy, lack of energy, psychomotor slowing and irritability, but with less guilt than is seen in patients without Parkinson's but with depression. Patients do tend to respond to SSRIs. Many are helped with psychotherapy, meditation and mindfulness.

Pain is often overlooked in Parkinson's as it can be difficult to identify as part of Parkinson's disease versus another etiology. It can be seen along with motor fluctuations. If patients complain of tingling or pain when they are getting closer to the end of their medication dose, then the symptoms are probably related to medication wearing off. If

the pain responds to levodopa, it's likely Parkinson's related. If the pain responds to anti-inflammatories or other pain medications, it's more likely due to non-Parkinson's musculoskeletal etiology.

Conclusion

Parkinson's disease involves more than just the motor symptoms associated with the loss of dopamine neurons. Parkinson's can offer a very complex clinical picture and patients often need a lot of time or frequent visits to address all of their issues. If the non-motor symptoms are not addressed, the motor symptoms will ultimately be harder to treat, making it essential to try to treat both motor and non-motor complaints in these patients.

For more information on the Santa Barbara Neuroscience Institute at Cottage Health, visit www.cottagehealth.org/neuro

CASE STUDY: Parkinson's Patient with Several Non-Motor Symptoms

A 65-year-old man with Parkinson's disease who was diagnosed five years ago, presents to clinic with relatively well-controlled symptoms. He is on Ropinirole 8mg TID. The patient states that he is doing fairly well. Otherwise, he says little.

At his next appointment, his wife mentions that he has been gambling more than before and has lost \$10,000 in the last month. Upon further questioning, the patient admits that he has been getting up at night to gamble online and he has actually lost more money than his wife thinks. Because Ropinirole is often implicated in impulse-control disorders, the patient is taken off the medication. His gambling behavior improves.

His motor symptoms are well controlled on Sinemet 25/100, two tablets, QID for about three years. As his motor symptoms progress, his Sinemet dose is increased and his dyskinesias also increase with more head, trunk and arm movements. He also begins to have dizziness with standing, and has near syncopal episodes multiple times per week. This happens most frequently when he is getting out of bed or stands up too quickly, consistent with a diagnosis of orthostatic hypotension (OH).

Many patients with Parkinson's Disease have OH to at least a small degree. A sub-set of patients have it to such a severe extent that they are barely able to stand up. If severe OH is a presenting feature, other Parkinsonian syndromes like Multiple Systems Atrophy should be considered. If OH is diagnosed later on in the course, it is more consistent with classic PD.

Some patients can experience such fluctuations in blood pressure that a short-acting antihypertensive is needed at night in conjunction with the daytime medications noted above. The dose should be stopped in the early afternoon to prevent blood pressure increases at night. Because the fluctuations are often complicated, working with a cardiologist can be helpful to determine the appropriate dosing and medications to use.

The patient is initially treated conservatively with increased fluids, use of compression stockings, discontinuing his Lisinopril and increased salt intake. Midodrine up to 10 mg TID or Fludrocortisone up to 0.6 mg QD is considered but Droxidopa (Northera), which is specifically approved for orthostatic hypotension in Parkinson's disease patients, is used instead with good success.



Saving The Brain continued from page 6 aspects and clinical features of stroke in women. This topic is of great importance since, despite our national pushes toward gender “equality,” we need to realize that the physiology and genetics of men and women are quite different, and it may be suboptimal to extrapolate therapies to both sexes equally.

Arbi Ohanian, MD, CMO of the Sage Management Group which provides neurohospitalist coverage for Cottage Health, explained how the neurohospitalist subspecialty of neurology has developed over time, and what an important role it plays in the support of acute stroke and inpatient neurology care. His insight into how this system can be used effectively has quite literally maintained the stroke programs of multiple California medical centers.



Left to Right:
Dr. Tom Jones,
Dr. Phil Delio,
Dr. Henry Marsh
(keynote speaker)

A particularly captivating talk was provided by **Pamela Jones, MD**, recently appointed to the neurosurgical faculty at the University of California, San Diego. Dr. Jones, in the footsteps of her father Dr. Tom Jones, is at the forefront of the latest techniques in the management of pituitary tumors, and we were lucky to have her share that expertise, in what was arguably the most technically advanced presentation we have seen to date at our symposium.

Our very own **Virginia “Ginny” Clay, RN**, Stroke Coordinator for Santa Barbara Cottage Hospital, gave a wonderful presentation on tele-neurology and stroke outreach, and was kind enough to formally recognize all the outside programs and hospitals who attended our annual symposium. It was impressive to note how much of our audience was from outside our local community, and she underscored the importance of our working as a Central Coast stroke team. Her coordination efforts in this regard have been a great asset to Santa Barbara Cottage Hospital.

Always entertaining, **John Park, MD, PhD**, Medical Director of the Brain and Spinal Tumor Program at SBNI, discussed the use of our novel iMRI to manage complex brain tumors operatively. Seeing how much the neuro-oncology program has developed under the direction of Dr. Park in the few short years since his arrival has been impressive and the Santa Barbara Neuroscience Institute at Cottage Health is fortunate to have his clinical expertise.


We were particularly lucky this year to have **Frank M. Longo, MD, PhD**, Professor and Chairman of Neurology

and Neurological Sciences at Stanford University School of Medicine, discuss his current research on Alzheimer’s disease. His pharmaceutical agent in development made the cover of Time magazine earlier this year, and he offered tremendous insight into the current trends in dementia care. More importantly, he did much to debunk all the dementia “remedies” currently circulating in the community, and we are waiting with baited breath in hopes that his new drug proves to be as successful in clinical trials as it has been to date in the animal models.

Finally, **Robert Taylor, MD**, Medical Director of Santa Barbara Cottage Hospital’s neuro-critical care unit, showed a series of cases highlighting the latest interventional techniques in acute stroke and endovascular care. This field has come a long way in five years. We can now consider it standard of care for many conditions including stroke and aneurysm treatment, and his examples demonstrate how well Cottage currently does with these complex disorders, conditions which traditionally would have been referred to large academic centers for management.

My own presentation covered the year in review for stroke treatment and care. With the help of our planning and coordinating committee members, all of whom I recognize here for their contributions and efforts, I am confident next year’s symposium – our 10th annual – will once again be exceptional.

For more information on the Santa Barbara Neuroscience Institute at Cottage Health, visit www.cottagehealth.org/neuro



**"Cottage's iMRI technology
offered me a different path to treat
my brain tumor."**

*Shortly after her procedure, Corby was
back to hiking her favorite trail.*

Corby Santa Maria

When doctors diagnosed Corby with a brain tumor they believed was difficult to treat, they recommended an intraoperative magnetic resonance imaging procedure (iMRI). The Santa Barbara Neuroscience Institute at Cottage is one of just a handful of hospitals in the nation that offer this specialized technology. Our advanced imaging system provides neurosurgeons with the clearest images during brain surgery, helping them remove the most difficult to treat tumors. The iMRI technology provides some patients with a different path and helps reduce the likelihood of an additional procedure.