# Vagus Nerve Stimulation Therapy

# The ILAE consensus statement on the definition of drug-resistant epilepsy

- For the first time, the epilepsy community has agreed on a working definition for refractory epilepsy
- The ILAE published the consensus definition in an effort to improve patient care and facilitate clinical research

# ILAE definition of drug-resistant epilepsy

- The failure of two appropriately chosen and tolerated AEDs (whether as monotherapies or in combination) to control seizures when used for an adequate period of time
- Defining the terms
  - Appropriateness: treatment should be proven (ideally in an RCT) to be effective for the patient's epilepsy and seizure type
  - Adequate: treatment used at adequate strength/dosage for a sufficient length of time
  - Seizure outcome: categorized as seizure free, treatment failure, or undetermined
  - Seizure free: no seizures including auras for at least three times the longest preintervention interseizure interval or 12 months, whichever is longer, with any other outcome considered a treatment failure

Kwan P, et al. *Epilepsia* 2010;51(6):1069:1077.

# What is refractory epilepsy?

- After adequate trials of at least 2 AEDs,[1] overall remission* rates with subsequent treatment trials are dramatically decreased[2]
  - 46% with the first treatment
  - 10.1% with the second treatment
  - 2.3% with the third treatment
  - 0.8% of patients responded optimally to further trials
- Diagnosis of refractory epilepsy becomes apparent within a few years of starting treatment[2]

1. Kwan P, et al. *Epilepsia* 2010;51(6):1069:1077.
2. Mohanraj R and Brodie MJ. Eur J Neurol. 2006;13:277-282.

# The consequences of refractory epilepsy are numerous[1,2]

- Seizure-related injuries[1,3]
- Increased seizure severity[3]
- Adverse effects with long-term AED use[1,3,5]
- Depression and anxiety[1,3,4]
- Cognitive and memory impairment[1,3,5]
- Increased mortality and morbidity[1,6,7]
- Increased healthcare utilization (eg, ER visits, hospitalizations)[8,9]
- Impaired ability to obtain education, to work, drive, establish families, and develop and maintain social relations[2,3]

1. Schmidt D. Epilepsy Res 2002;50:21-32. 2. Wheless JW. Epilepsy Behav 2006;8:756-764. 3. Fisher RS, et al. Epilepsy Res 2000;41:39-51. 4. Gilliam F. Neurology 2002;58:S9-S20. 5. Meador KJ. Neurology 2002;58(suppl 5):S21-S26. 6. Lhatoo SD, et al. Postgrad Med J 1999;75:706-709. 7. Annegers JF, et al. Epilepsia 1998;39:206-212. 8. Faught E, et al. Epilepsia 2009;50:501-509. 9. Lee WC, et al. Clin Ther 2005;27(10):1629-1638.

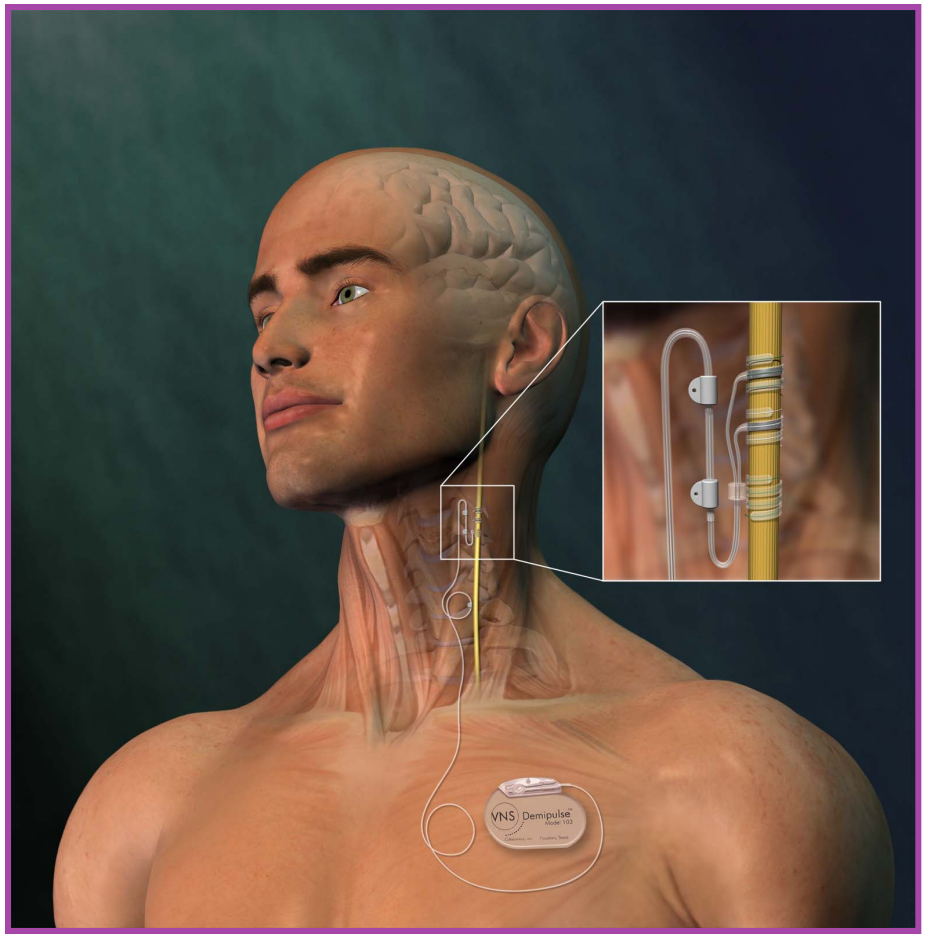
# In refractory epilepsy, nonpharmacologic options are needed

- Despite 14 new AEDs entering the market in the last 15 years, the rate of refractory epilepsy has not been significantly reduced[1]
- Refractory epilepsy seems like a different disease compared with easy to control epilepsy, and new strategies are needed to help these patients[2]
- Just extending the use of drugs in refractory epilepsy is not appropriate[2]

1. Brodie MJ, Schachter SC, and Kwan P (eds). Fast Facts: Epilepsy. Health Press, 2010. 2. Schmidt D. Epilepsy Res 2002;50:21-32.

# What is VNS Therapy?

The VNS Therapy System consists of an implanted pacemaker-like generator and nerve stimulation electrodes, which deliver intermittent stimulation to the patient's left vagus nerve that sends signals to the brain.



# On-demand magnet stimulation is a unique benefit of VNS Therapy

- Offers more control for patients and their families[1,2]
- Initiates on demand stimulation
  - May abort or decrease severity of seizures[1-3]
  - May improve postictal period[2]
- Stops stimulation
  - Acutely manage side effects[3]

1. Boon P, et al. J Clin Neurophys. 2001;18:402-407. 2. Fromes GW, et al. Epilepsia. 2000;41(suppl 7):117. 3. Schachter SC and Saper CB. Epilepsia. 1998;39:677-686.

# VNS Therapy has a unique side effect profile

- Most side effects associated with VNS Therapy
  - Occur only during stimulation[1,2]
  - Generally diminish over time[2]
  - May be diminished or eliminated by the adjustment of parameter settings[2]
  - May be controlled by use of the magnet[3]
  - Similar across age groups[4,5]

1. Ben-Menachem E, et al. Neurology. 1999;52(6):1265-1267. 2. Ben-Menachem E. J Clin Neurophysiol. 2001Sep;18(5):415-418. 3. Schacter SC. Neurology. 2002;59(suppl 4):S15-S20. 4. Alexopoulos AV, et al. Seizure. 2006;15(7):491-503. 5. Sirven JI, et al. Neurology. 2000;54:1179-1182.

# VNS Therapy is a proven treatment with a unique safety profile

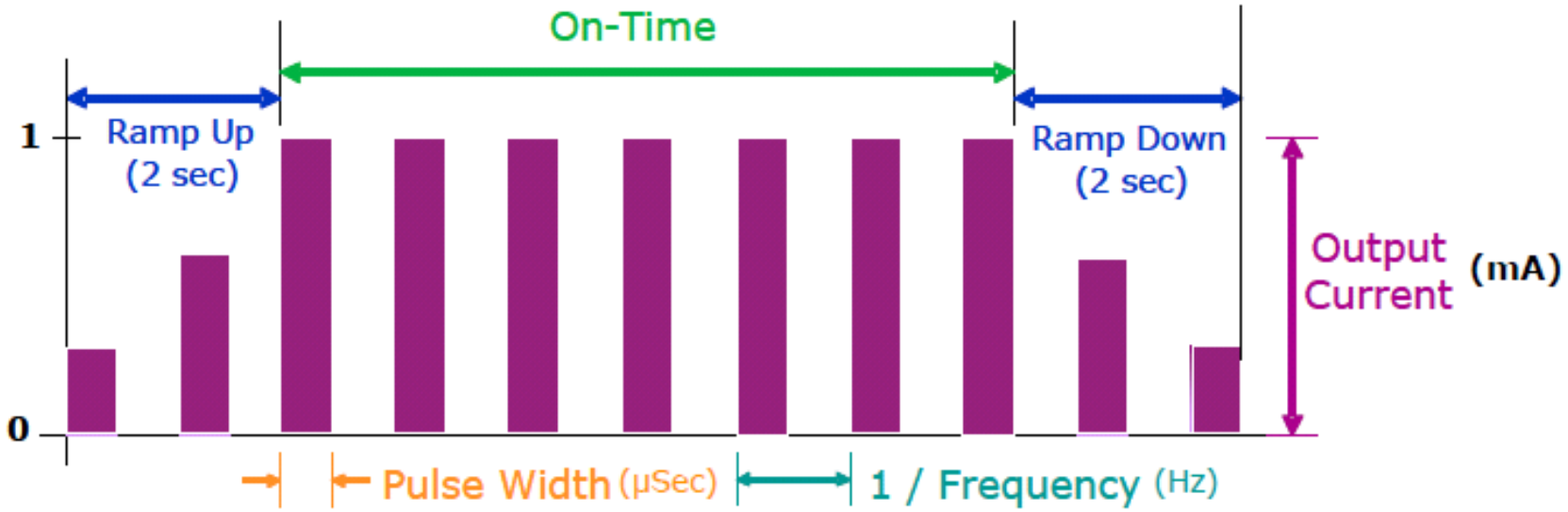
- More than 60,000 patients worldwide have been implanted with VNS Therapy
- No known interactions with medications
- No reported systemic neurotoxic effects, rash, renal impairment, or bone marrow suppression
- No increase in sudden, unexpected death in epilepsy (SUDEP)[1]
- Gestational outcomes
  - Animal study has shown no evidence of impaired fertility or harm to the fetus due to VNS Therapy[2,3]
  - Pregnancies have gone to term with VNS[4,5]

1. Annegers JF, et al. Epilepsia. 1998;39:206-212. 2. Physician's Manual. Houston, TX: Cyberonics, Inc. 3. Danielsson et al. 4. Ben-Menachem E, et al. Epilepsia. 1998;39(6):180. 5. Husain MM, et al. Ann Gen Psychiatry. 2005;4:16.

# Several parameters can be adjusted to individualize treatment[1]

- Each parameter can be independently programmed, thereby offering multiple setting combinations from which optimal stimulation for the patient can be selected[1]

- Safe and effective VNS Therapy is dependent primarily on output current, signal frequency, pulse width, ON/OFF time[2]




1. Physician's Manual. Houston, TX: Cyberonics, Inc. 2. Heck C, et al. *Neurology* 2002;59(Suppl 4):S31-S37.