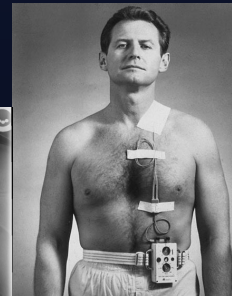
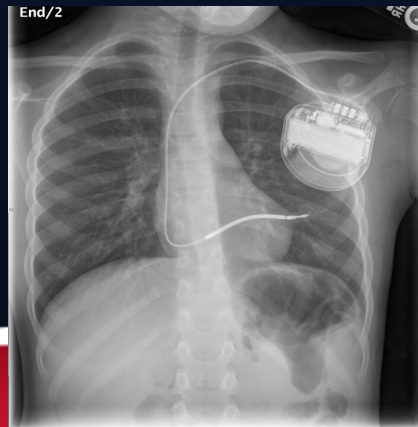


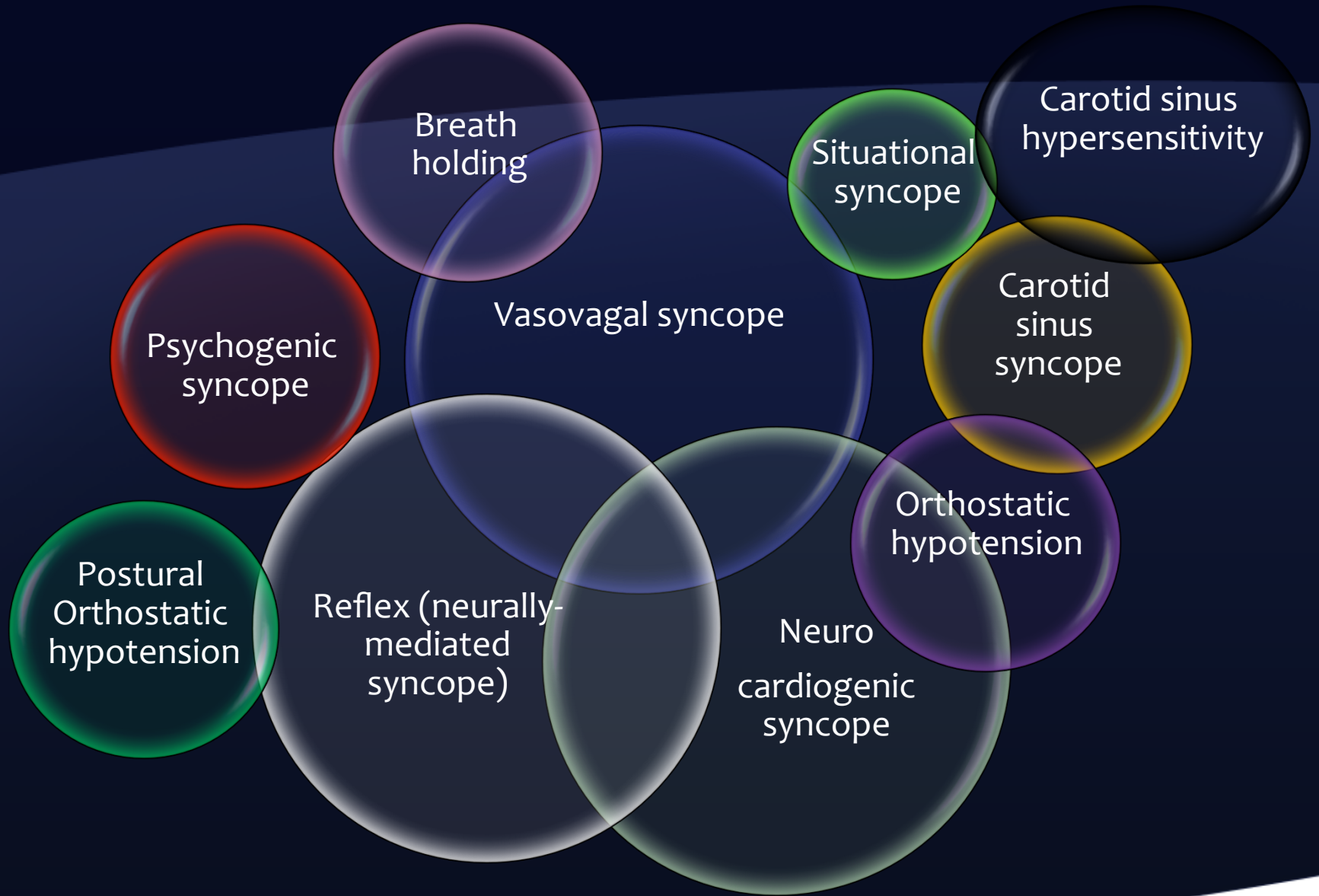
Pacing for Vasovagal Syncope: We can but when should we?



Susan P. Etheridge, MD, FHRS, CEPS
University of Utah



UNIVERSITY OF UTAH
SCHOOL OF MEDICINE



Pacing in Vasovagal Syncope

- Sound idea – prevent bradycardia that can occur as a part of vasovagal syncope
- What can adult trials teach us?
- Can we choose the correct patients and for this invasive and expensive technology?



Vasovagal Syncope

Complex cardiac and central nervous system reflex arc with many components

- Reflex vasodilation and bradycardia are 2 main mechanisms often acting together
- Often preceded by trigger -orthostatic stress – upright posture, venous pooling
- Ineffective venoconstriction and decreased venous return, cardiac output and cerebral perfusion



Vasovagal Syncope

- Not always clear when bradycardia occurs in the process and how much it contributes
- May be different in each patient
- Response to therapy may be different
- Vasodilatation may still cause fainting, even after bradycardia is prevented by pacing



Toddlers



Elderly



Teenagers



The Burden of Syncope

further characterized by rapid onset, brevity, and spontaneous recovery.¹ It is a common presentation to the emergency department, accounting for $\approx 1\%$ of attendances.^{2,3} In the United States, 30% to 40% of such patients are subsequently admitted for further investigation at an annual cost of \$2.4 billion according to the Medicare database.^{2,4-6} This relates to multiple expensive, low-yield investigations and unnecessary hospital admissions.¹ Beyond the economic impact, recurrent syncope is associated with significant

Saklani Circ 2013, Alshekhlee Am J Med. 2009, Sun. Am J Cardiol 2009



UNIVERSITY OF UTAH
SCHOOL OF MEDICINE

Goals of Therapy

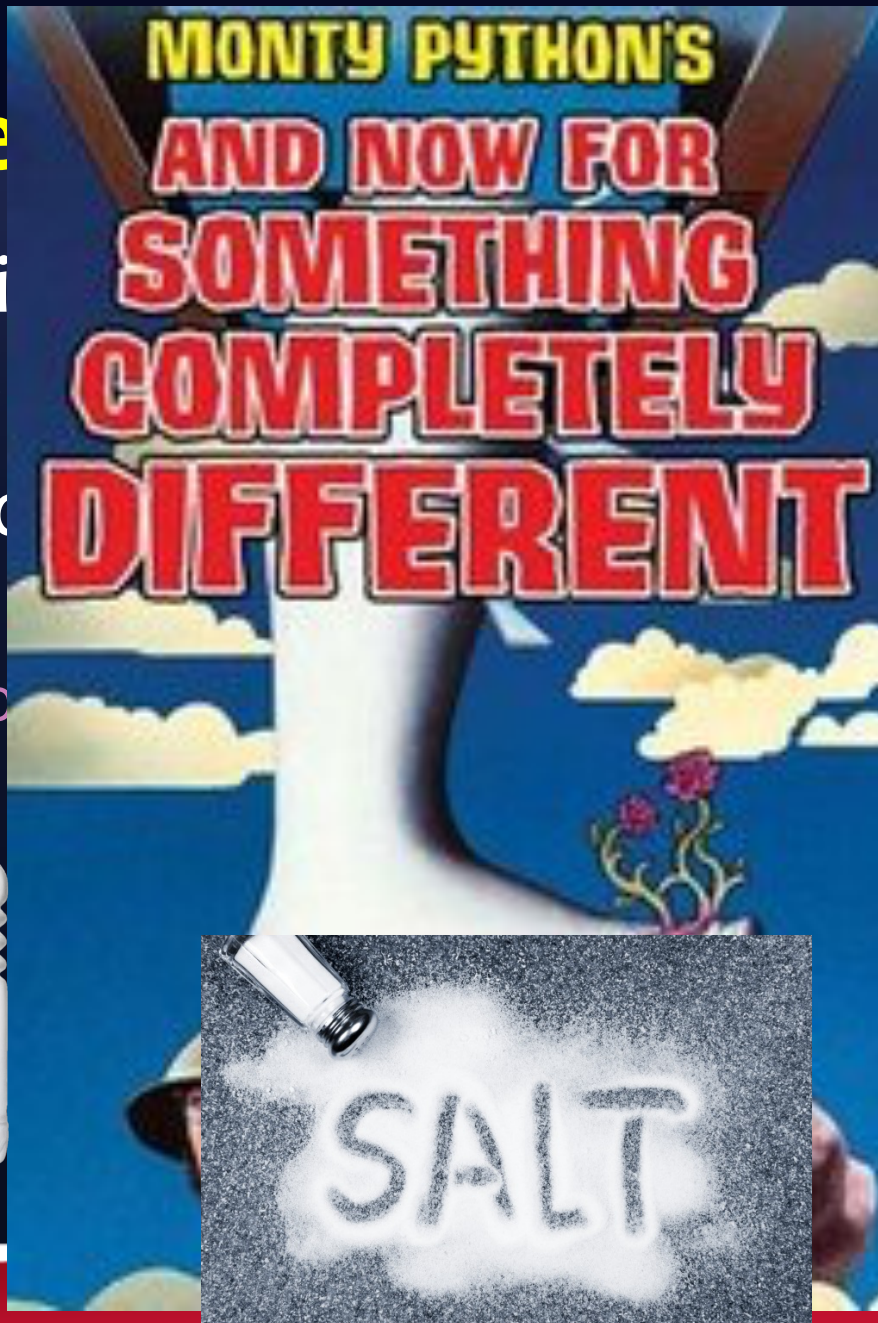
- Reduce events
 - Especially in high risk populations- pilots, commercial drivers
- Avoid physical trauma
- Improve quality of life



Prove

- Nonmedicinal proven or
- Drug studies benefit

Mido



elusive

ded but not

ent clinical

Disopyramide
kers

Fludrocortisone



SCHOOL OF MEDICINE

AH

THE LANCET

Volume 333, Issue 8639, 25 March 1989, Pages 658–660

Originally published as Volume 1, Issue 8639

Hospital Practice

TILTING TOWARDS A DIAGNOSIS IN RECURRENT UNEXPLAINED SYNCOPE

A Fitzpatrick R Sutton

- HUT in 71 patients
- Temporary dual-chamber pacing aborted syncope in 85% and improved cardiac index and systemic blood pressure during tilt
- So maybe syncope patients will benefit from pacing



UNIVERSITY OF UTAH
SCHOOL OF MEDICINE

1993



The NEW ENGLAND JOURNAL of MEDICINE

HOME

ARTICLES & MULTIMEDIA ▾

ISSUES ▾

SPECIALTIES & TOPICS ▾

FOR AUTHORS ▾

CME >

ORIGINAL ARTICLE

Comparison of Cardiac Pacing with Drug Therapy in the Treatment of Neurocardiogenic (Vasovagal) Syncope with Bradycardia or Asystole

Jasbir S. Sra, Mohammad R. Jazayeri, Boaz Avitall, Anwer Dhala, Sanjay Deshpande, Zalman Blanck, and Masood Akhtar
N Engl J Med 1993; 328:1085-1090 | [April 15, 1993](#) | DOI: 10.1056/NEJM199304153281504

- Study designed to assess efficacy of pacing in preventing hypotension induced by head-up tilt



UNIVERSITY OF UTAH
SCHOOL OF MEDICINE

Results

- Bradycardia was consistently preceded by hypotension
- Pacing did not prevent hypotension and syncope during tilt testing
- Bradycardia plays only a secondary part in pathogenesis

Conclusions. In patients with neurocardiogenic syncope associated with bradycardia or asystole, drug therapy is often effective in preventing syncope, whereas artificial pacing is not. (N Engl J Med 1993;328:1085-90.)



1994-1998..... they keep trying...

- Possible role in selected patients with malignant cardioinhibitory syncope
 - Small numbers 12-37 patients
 - Improvement in 78-93% and many with resolution
 - Improved quality of life
 - ALL retrospective, uncontrolled
- call for randomized controlled studies



2000-2004 Randomized Studies in Pacing for Adult Syncope

- VPS, VASIS, SYDIT show reduction in syncope
- Unblinded... they knew they had a pacemaker
- “syncope has emotional triggers (smell, pain, disgust), and emotional reaction to receiving a pacemaker appears to have influenced outcomes importantly”



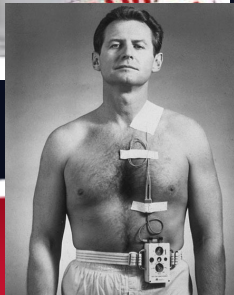
2004-2007 Blinded RCT Studies

- Everyone gets a pacemaker (VPS II and SYNPACE) - programmed on versus programmed off
- Double-blind RCTs fail to prove superiority of pacing over placebo
- Treating bradycardia component does not work because reflex vasodilation continues to cause the patient to faint



“Expectation Effect”

- Placebo effect of pacing
- Knowledge of the pacemaker leads to expectation of benefit (patient and physician)
- Outcome ascertainment bias based on awareness of the pacemaker



Pacing for Vasovagal Syncope

- Low quality evidence evidence for pacing in adult studies
- Roll for pacing remains controversial
- Vasodepressor role dominant over cardioinhibitory role



... but they keep at it

- But, trials included patients with cardioinhibitory *and* vasodepressor *and* mixed types of syncope

.....Maybe just choosing the wrong patients



Patient Selection

- Could pacing be effective for cardioinhibitory syncope with prolonged asystole?
- And... maybe tilt testing not a good way to predict (*good news*)
- Asystole should be documented at time of syncope ...
- ILR used to document asystole



ISSUE-2

- Syncope and asystole on ILR
- Pacemaker patients a 80% risk reduction of syncope recurrence in comparison with untreated groups
- ISSUE-2 was NOT controlled double-blind trial

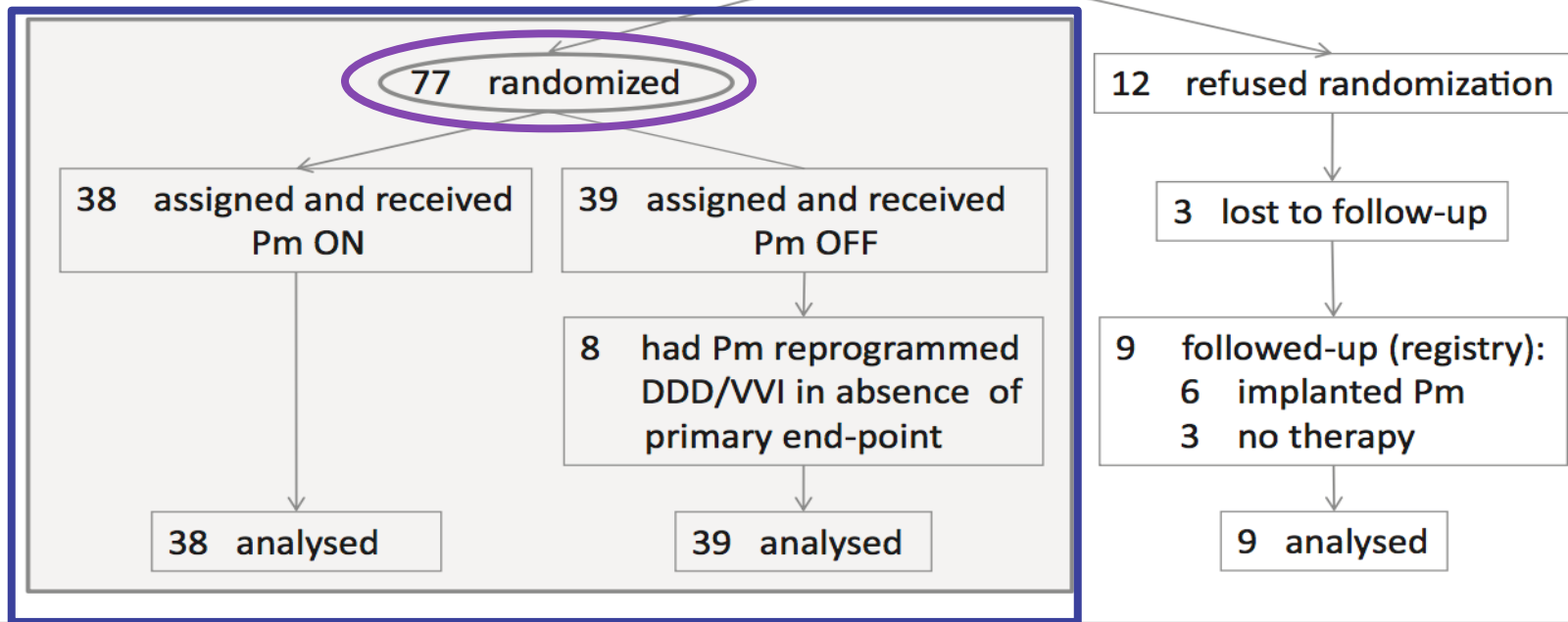


Screening phase

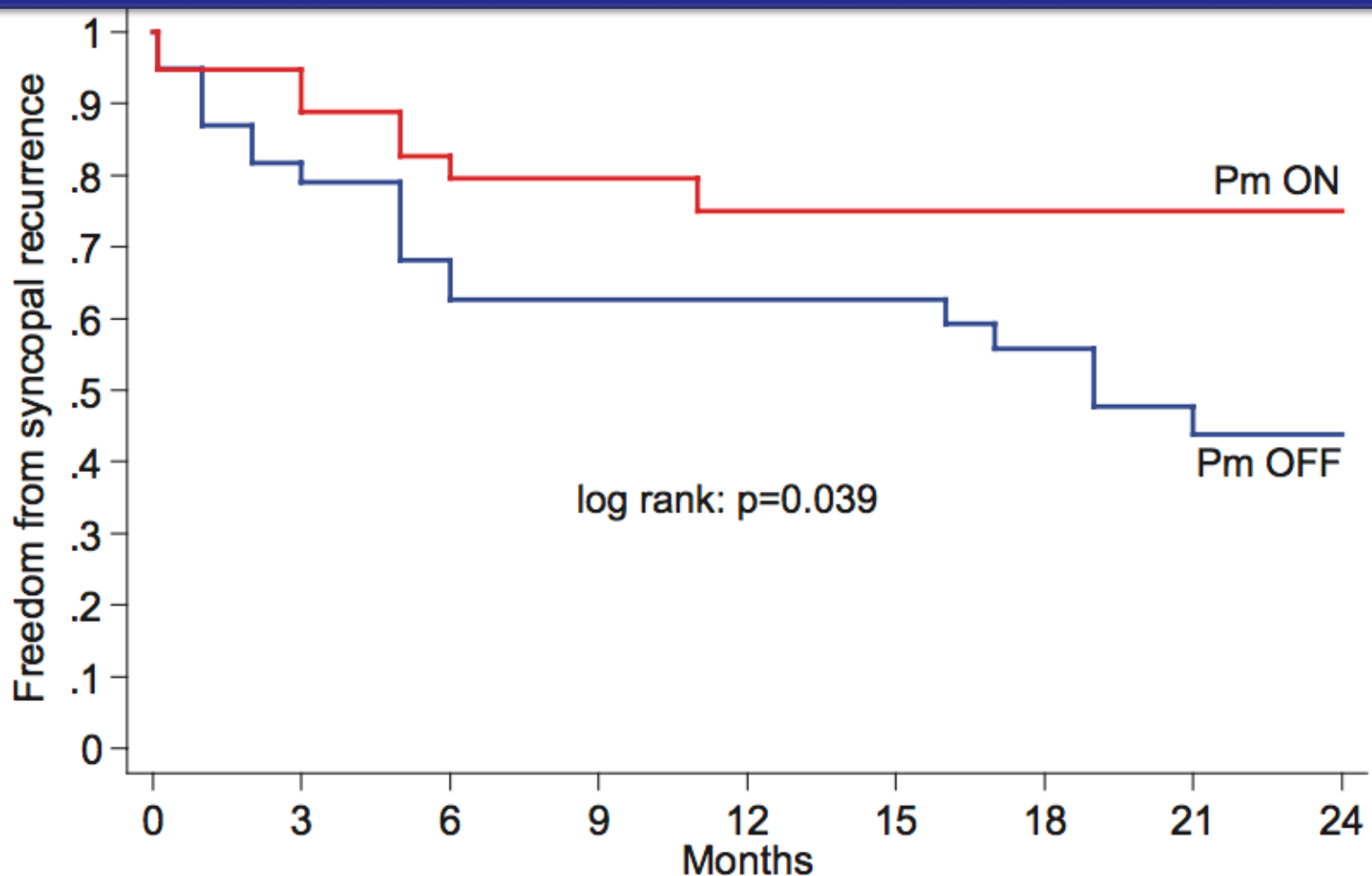
511 met inclusion criteria
and received an ILR

Study phase

89 had ECG documentation of:
- syncopal recurrence with asystole ≥ 3 s (#72)
or
- non-syncopal asystole ≥ 6 s (#17)



Syncopal recurrence rate higher with pacemaker OFF than with pacemaker ON (57% vs. 25%, $P = 0.039$)



Number at risk

Pm OFF	39	31	25	21	21	18	15	12	8
Pm ON	38	32	27	22	16	14	13	13	11



Finally

- Blinded RCT (ISSUE 3) demonstrated:
 - pacemaker is effective in preventing syncope recurrence
 - selected patients with cardioinhibitory response
 - documented by ILR
- Prevention could not be ascribed to a placebo effect
- Best news....tilt testing not helpful



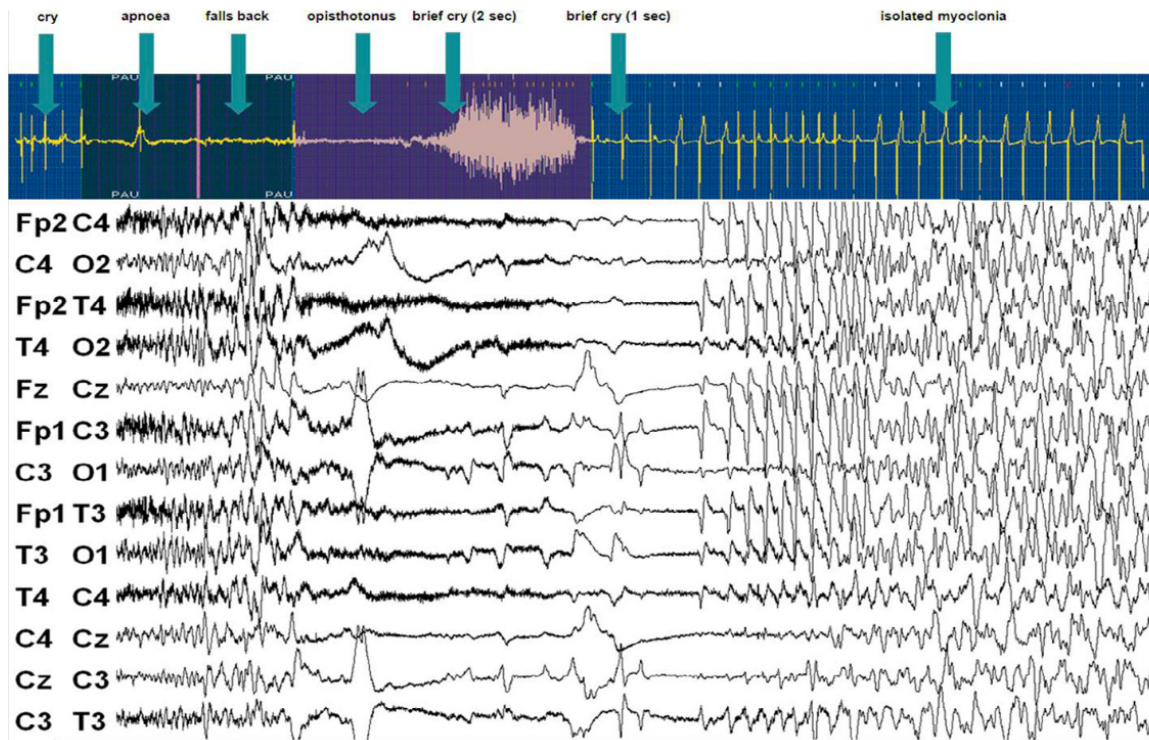
Pacing in Pediatric Syncope

- Role for young patients remains to be established
- Efficacy and cost issues
- Psychological sequelae and burden of long-term implanted device need to be justified
- Pacing may be considered for syncope or breath holding spells
- IIb



Pacing Breath Holding Spells

0.1-5% of children



UNIVERSITY OF UTAH
SCHOOL OF MEDICINE

Breath-Holding Spells

- Death reported, but rare
- Spells affect quality of life of family
- Pacing reported in case series
 - “spectacular with disappearance of spells and restoration of normal rhythm”*
 - “safe, efficacious and warranted”*
 - “should be considered in select patients after other treatments fail”*



Pacing for Breath-Holding Spells

- Expectation effect diminished
 - in the patient
 - maybe not in the physician or parent



Pacemaker in complicated and refractory breath-holding spells: When to think about it?

Stefano Sartori ^{a,*,1}, Margherita Nosadini ^{a,1}, Loira Leoni ^b, Luca de Palma ^a,
Irene Toldo ^a, Ornella Milanesi ^c, Alessia Cerutti ^c, Agnese Suppiej ^a

^a *Pediatric Neurology Unit, Division of Pediatrics, University of Padua, Padua, Italy*

^b *Cardiology Division, University of Padua, Padua, Italy*

^c *Pediatric Cardiology Unit, Division of Pediatrics, University of Padua, Padua, Italy*

Received 15 July 2013; received in revised form 2 February 2014; accepted 5 February 2014

- Review of 48 children in literature
- 90% failed medical therapy
- 38 (86%) complete resolution
- Decreased in the rest
- Complications of pacing in 26%

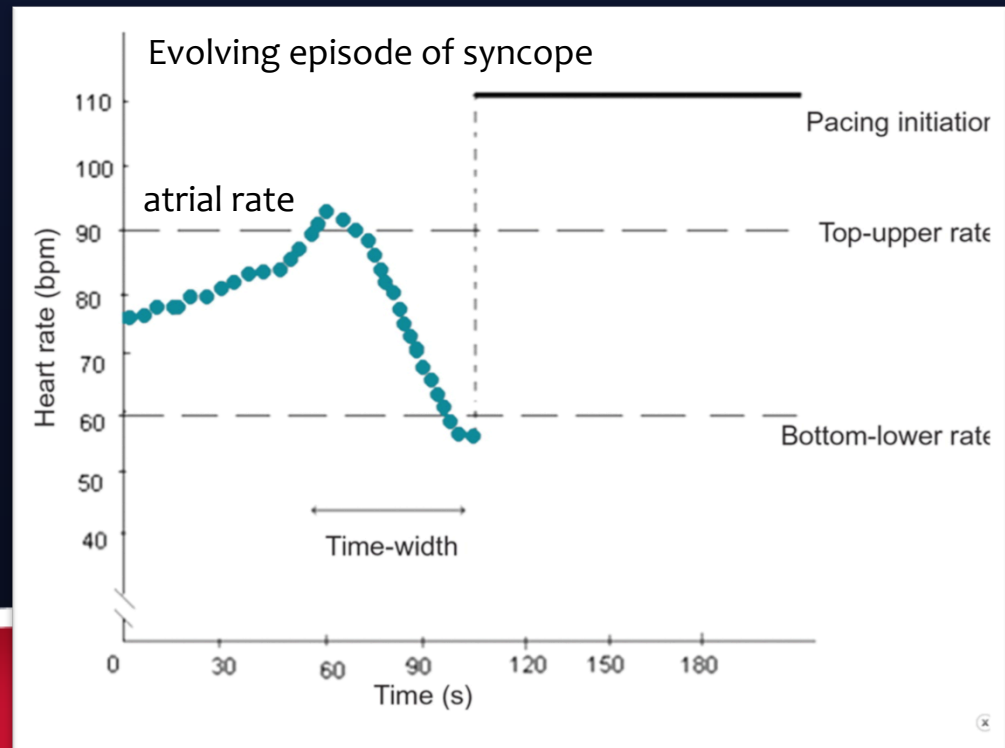
So you have decided to pace. What is the best pacing mode?

Ideally the device should sense and pace early at a relatively high rate for enough time but not too much



Rate Drop Pacing in Syncope

- Mode used in adult trials
- Rapid DDD pacing if device detects a rapid decrease in heart rate (DDD-RDR)
- device identifies a significant fall in heart rates
- suggests imminent syncope
- initiates high-rate pacing 110-120 bpm for 1-2 minutes



Closed-Loop Stimulation (DDD-CLS)

- Detects change in contraction dynamics in early phase of syncope
- Counteracts drop in blood pressure with an acceleration of heart rate



Why might the pacemaker fail?

- Vasodepressor > cardioinhibitory syncope
- Heart rate never low enough to trigger the pacemaker



Pacing in Syncope

- Effective \neq Necessary
- Context
 - benign condition
 - frequently affects young patients
 - can resolve
- Pacing should be a last resort
- Highly selected small proportion of patients



Placebo Effect... even from the ILR

- Useful in differentiating between different causes of loss of consciousness
- Reports have shown that ILR actually lowered likelihood of syncope by 30% -70%



When to consider?

- Should be considered in children with severe cardioinhibitory syncope in whom conventional treatment has not worked
- Noncompliant patients
- Recurrent symptoms, injury and asystole on monitoring



Pacing for Syncope in the Young

- Adult studies show benefit – most uncontrolled for placebo effect
- Significant commitment in young person
 - reserved for severe, frequent events
 - in whom drug therapy fails
- Reserved for those with profound bradycardia/asystole during spontaneous syncope (ILR)

