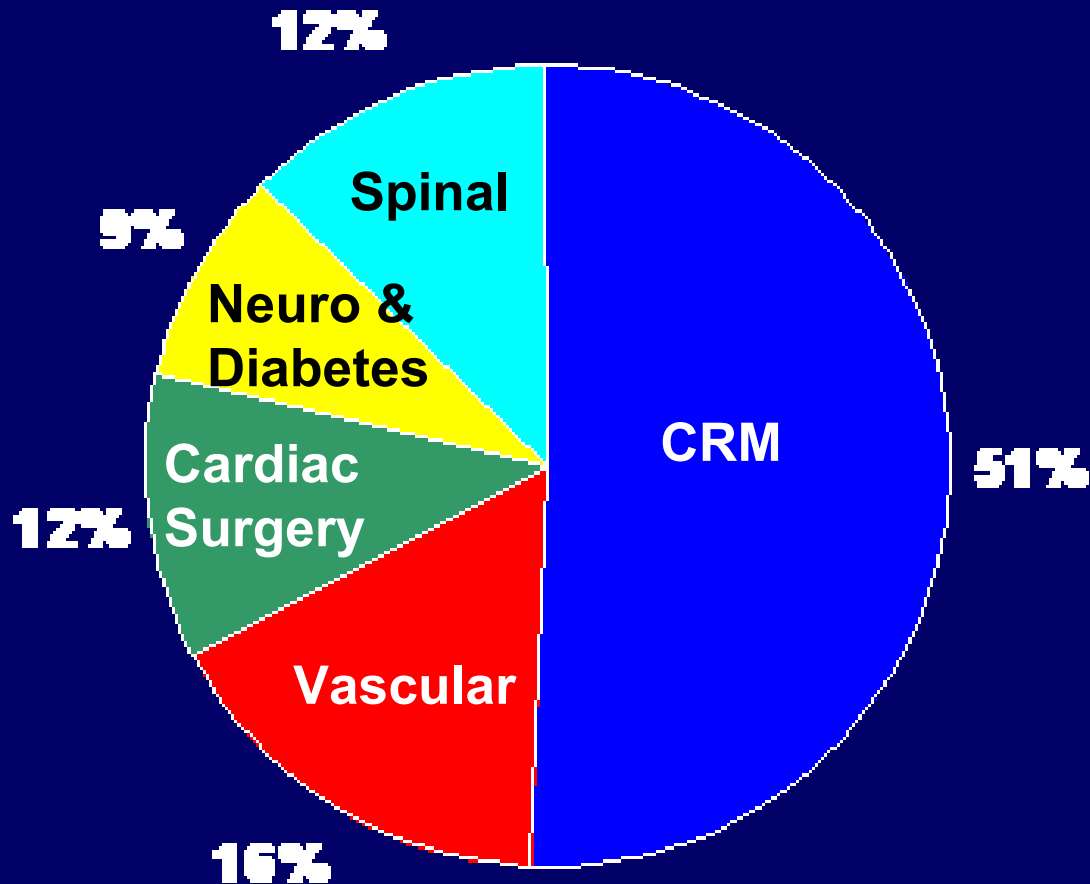


Cardiac Rhythm Management

Therapies, Products & Market Overview

CRM is Medtronic's largest business

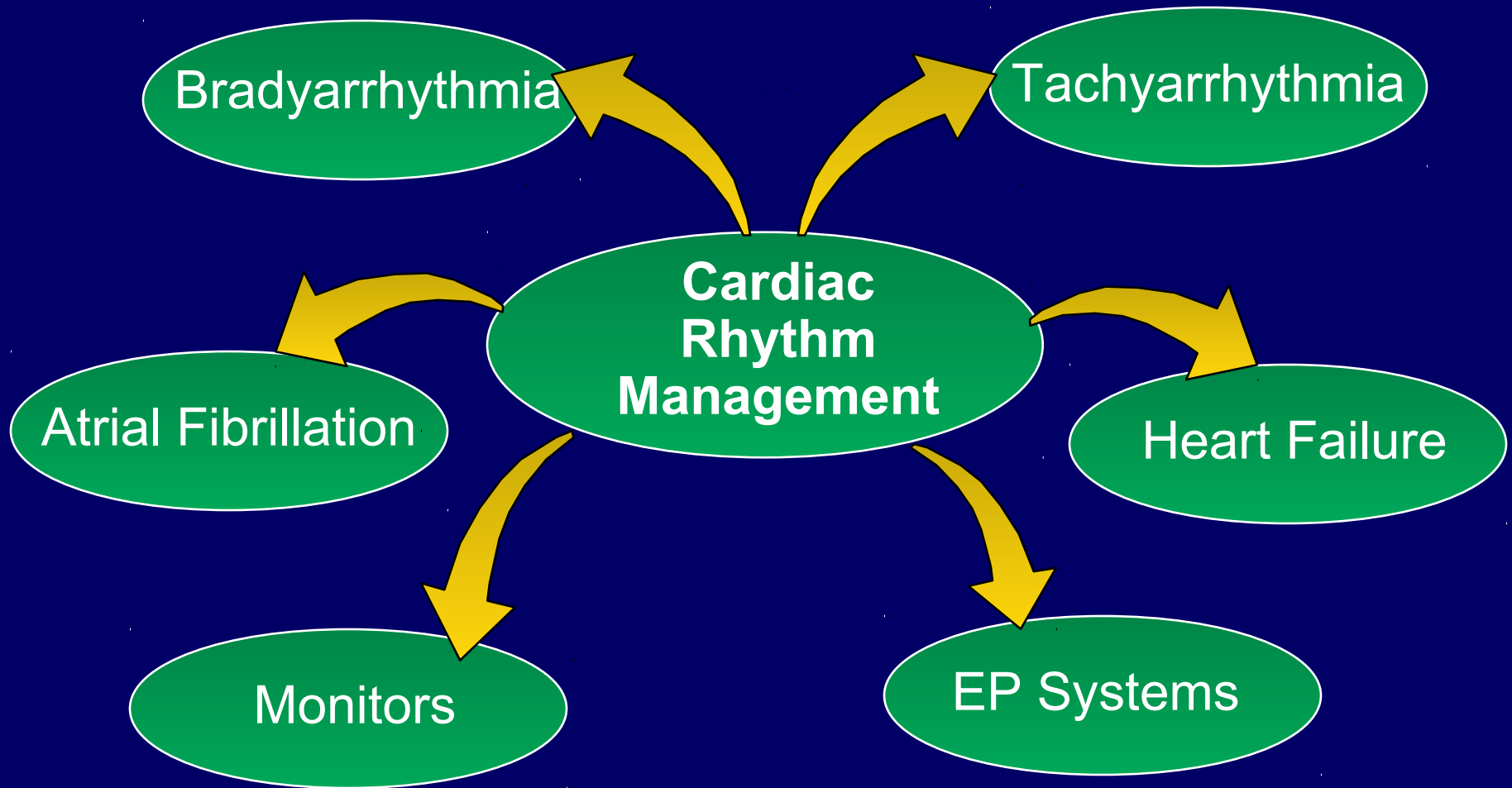


Western Europe Revenue: ~\$1.3 billion



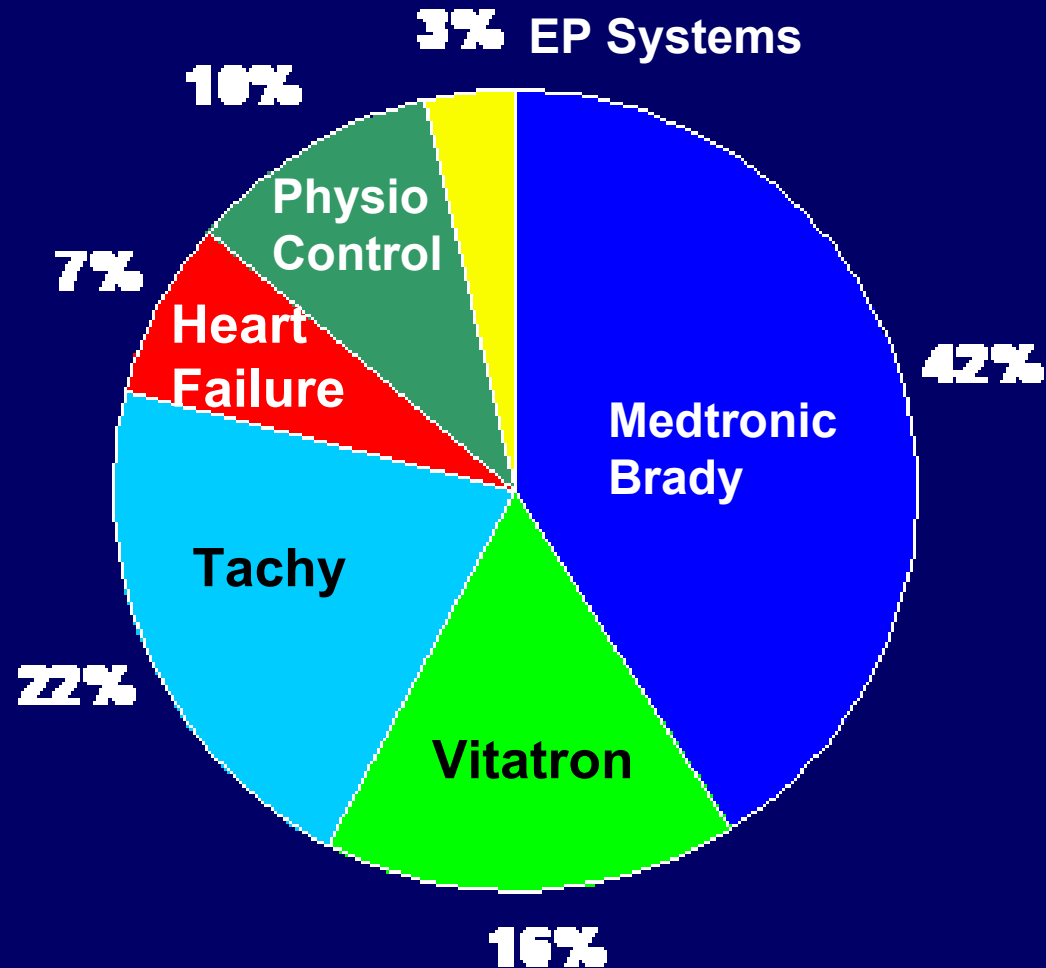
Medtronic

Cardiac Rhythm Management Businesses



Medtronic

CRM's businesses



Western Europe Revenue: \$650 million



Medtronic

Cardiac Rhythm Management

▣ Provides:

- Implantable Pulse Generators (IPG's)
- Implantable Cardioverter Defibrillators (ICD's)
- Programmers (+Patient Management Tools)
- Leads
- Monitors
- External Pacing Systems
- Electrophysiology Mapping and Ablation Systems

▣ For: Slow, Fast, Irregular and Failing Hearts

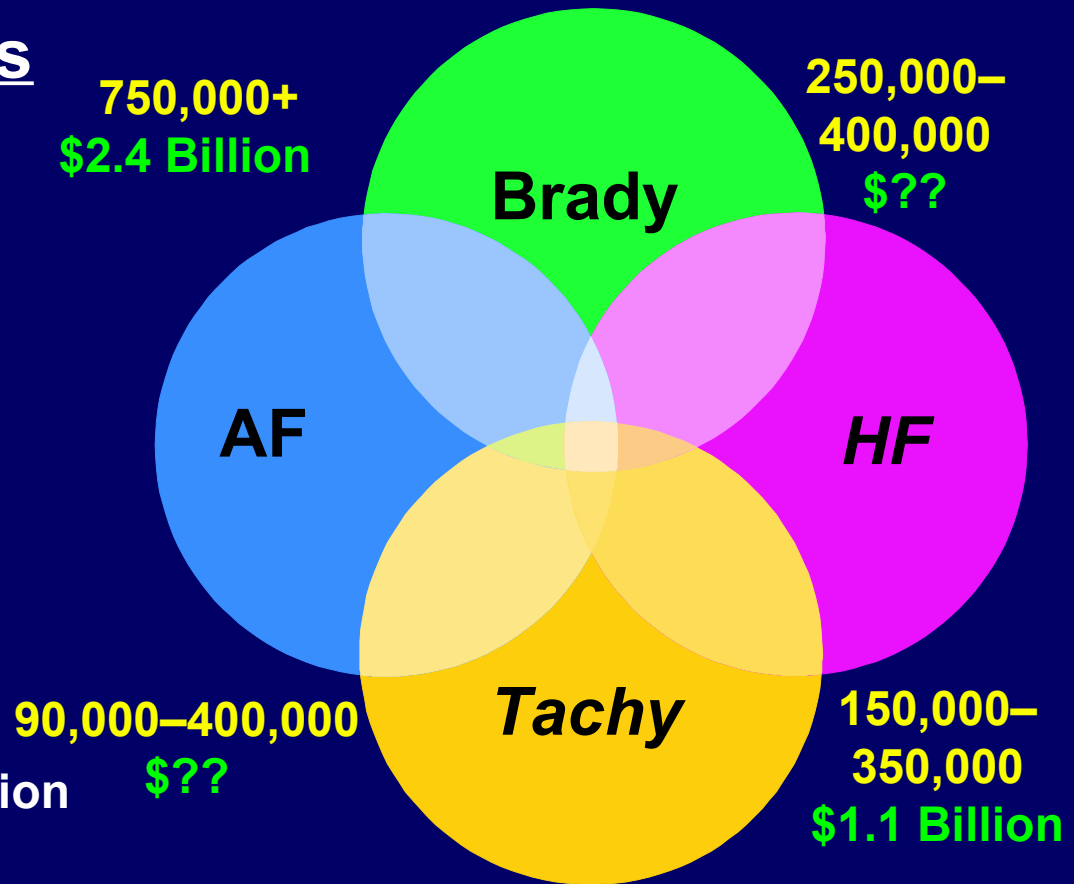
- Electrical and Mechanical indications

Cardiac Rhythm Management Strategies

Expanding Markets

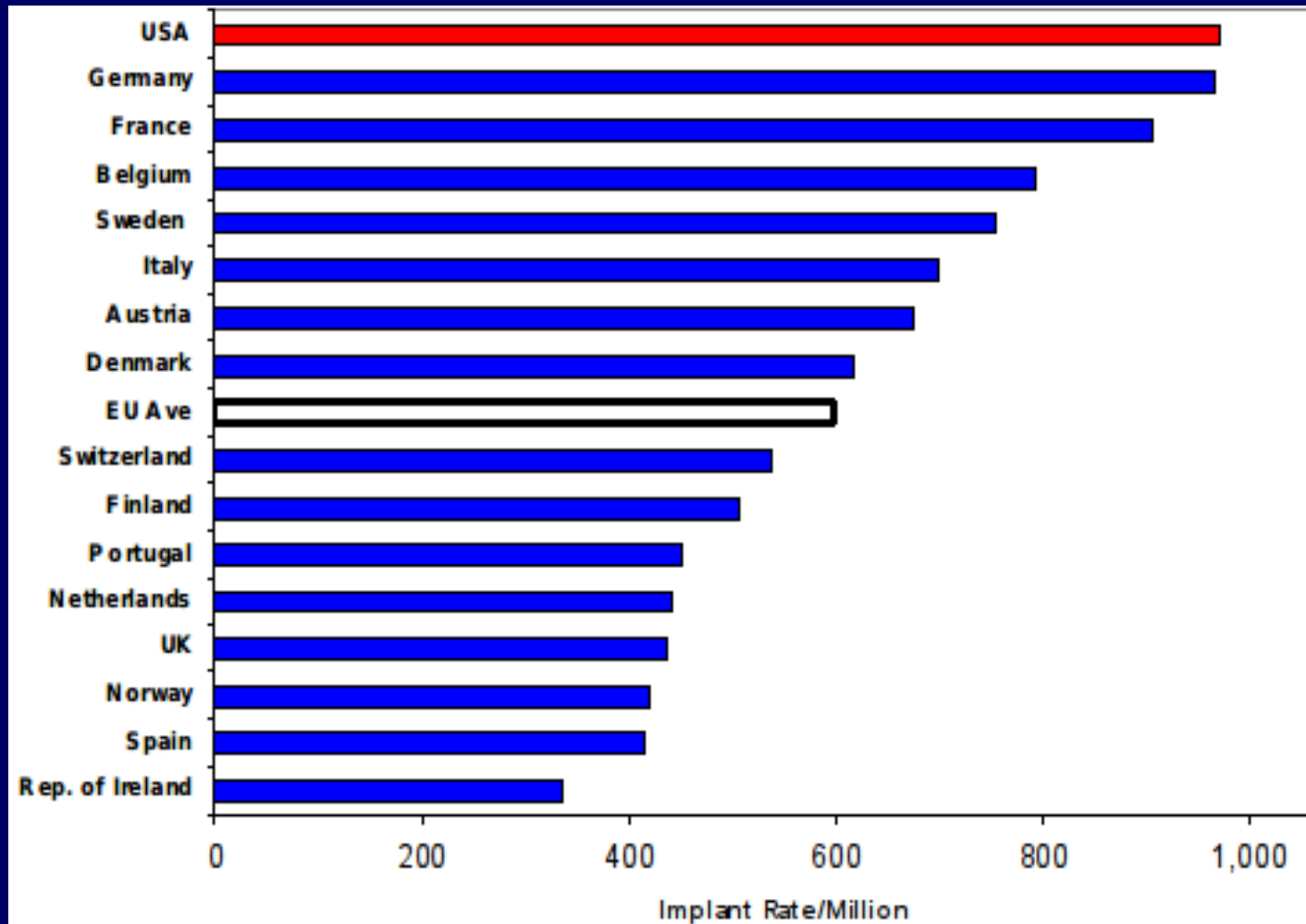
Apply combinations of core Medtronic technology to address disease states as they exist alone, as co-morbidities and as they progress

- Potential Patient Population
- Current Market Size

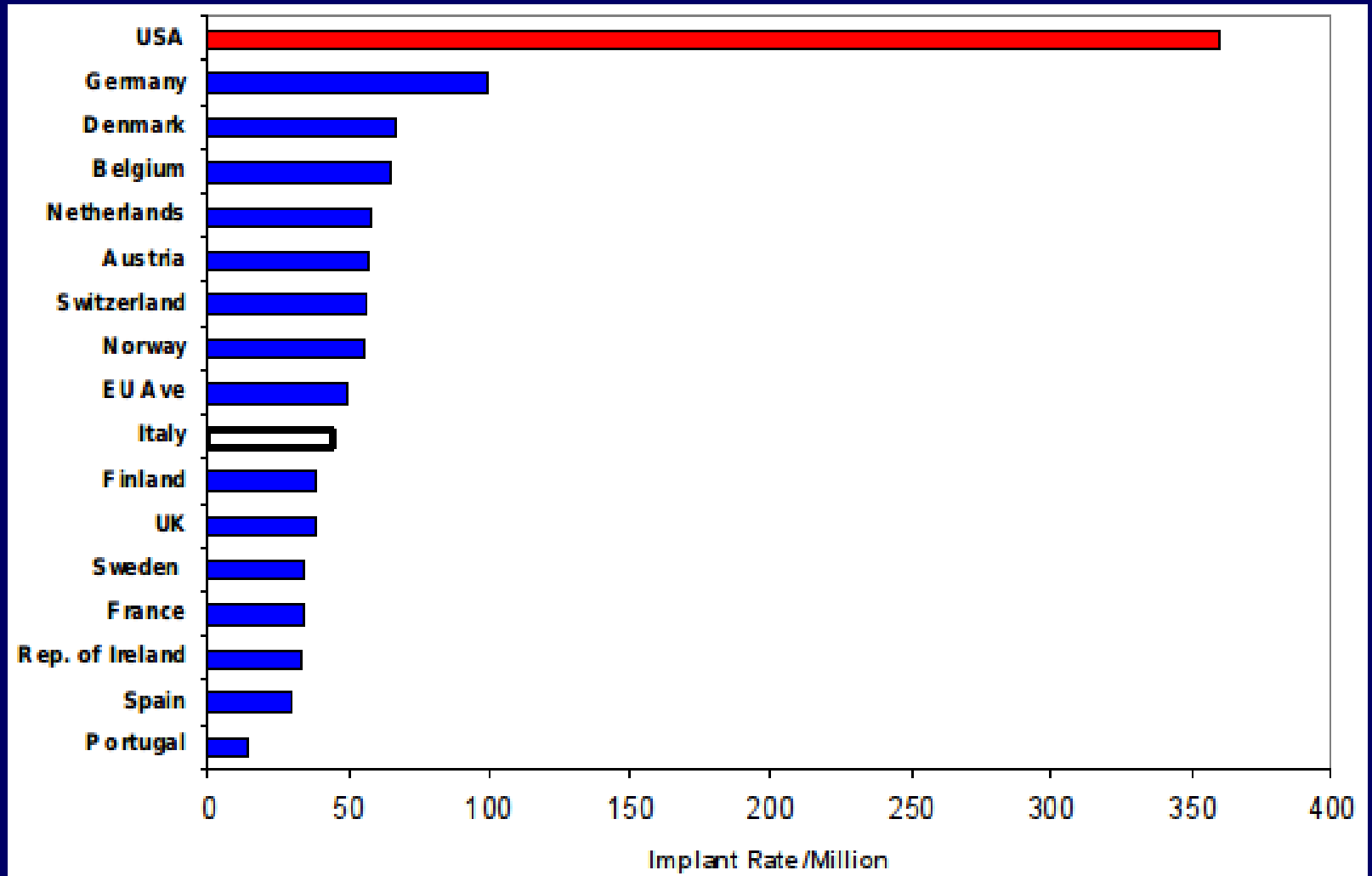


Medtronic

European IPG Implant Rates



European ICD Implant Rates



Bradyarrhythmia Management

The Clinical Problem

Who are the *traditional* patients requiring permanent pacing therapy?

- People with bradyarrhythmias
- Definition: **bradyarrhythmia**
 - A **slow** heart rate



...which can cause transient or permanent symptoms.

- Syncope (fainting)
- Pre-syncope
- Dizziness
- Fatigue
- Palpitations
- Mental confusion
- Exercise intolerance
- Seizure



If the symptoms include Syncope - What is Syncope?

▣ Syncope

- Sudden transient loss of consciousness
 - ▣ Associated with loss of postural tone
 - ▣ Due to abrupt reduction or loss of cerebral perfusion



The clinical impact can be significant.

- Reduction in QoL
- Falls and associated injuries
- Potential emergence of dangerous ventricular tachyarrhythmias that result from bradycardia



Recurrent, Unexplained Syncope: Quality Of Life Impact

Area of Impairment	Proportion Impaired
Anxiety/depression	73% ¹
Daily life activities	71% ²
Driving	60% ²
Physical activities	56% ²
Employment	37% ²
Sexual function	30% ²
Relationships with family, spouse, friends	28-30% ²

¹ Linzer M. *J Clinical Epidemiol.* 1991;44:1037-1043.

² Linzer M, et al. *J Gen Intern Med.* 1994;9:181-186.



Magnitude of the Problem

- **Syncope is a common clinical problem with significant costs**
 - Approximately 750,000 new patients per year in Europe (0.2% of the population)
 - 1-6% of hospital admissions²⁻⁴
 - 3% of emergency room visits per year⁵

1. National Disease and Therapeutic Index, IMS America, Syncope and Collapse ISC#780.2, Jan 1997-Dec 1997.

2. Gendelman HE, et al. *NY State J Med.* 1983;83:1161-1165.

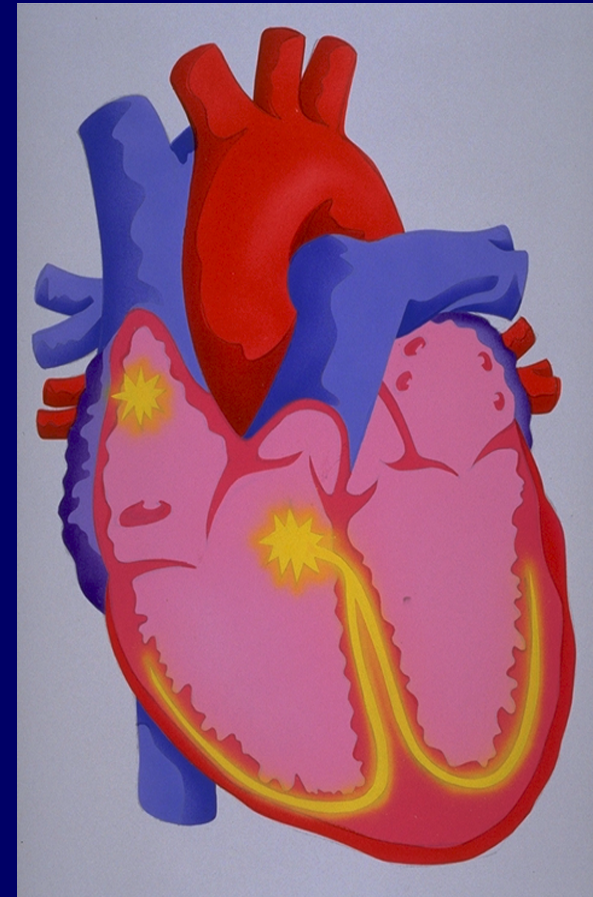
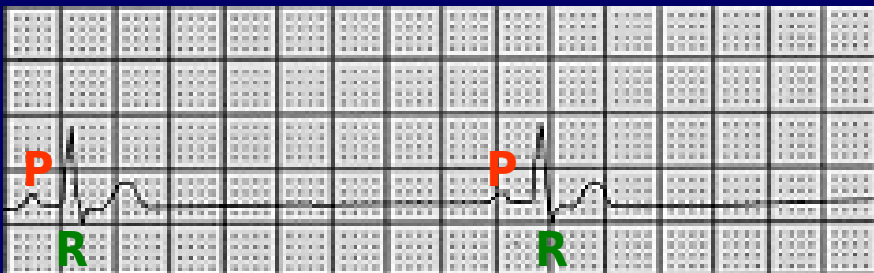
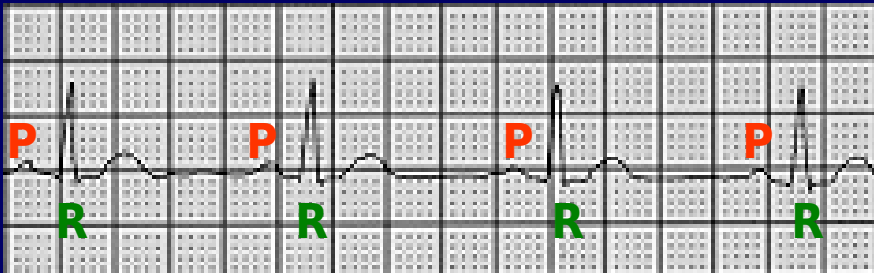
3. Kapoor W, *Med.* 1990;69:160-175.

4. Eagle K, et al. *Yale J Biol and Med.* 1983;56:1-8.

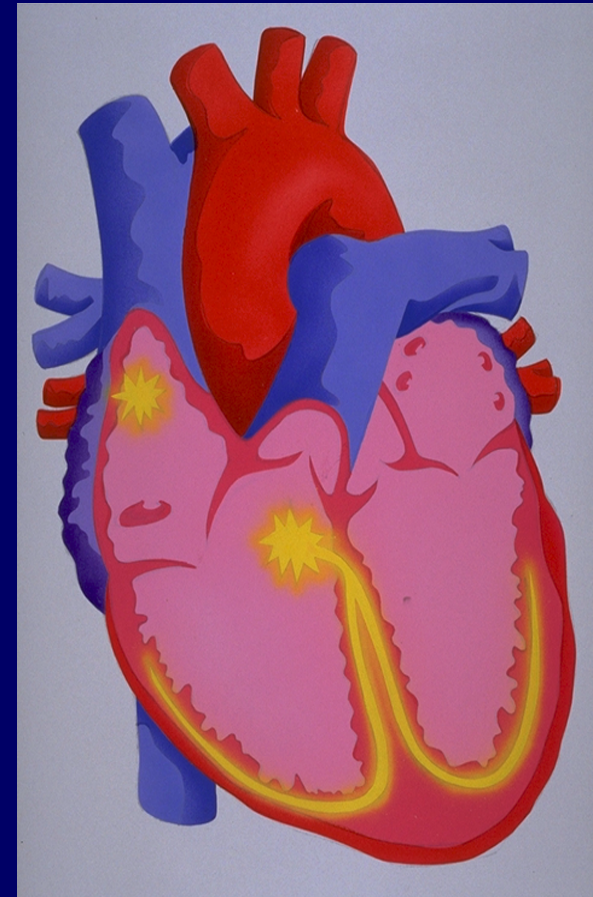
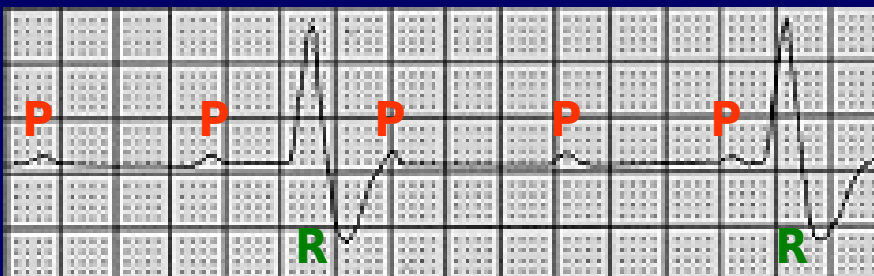
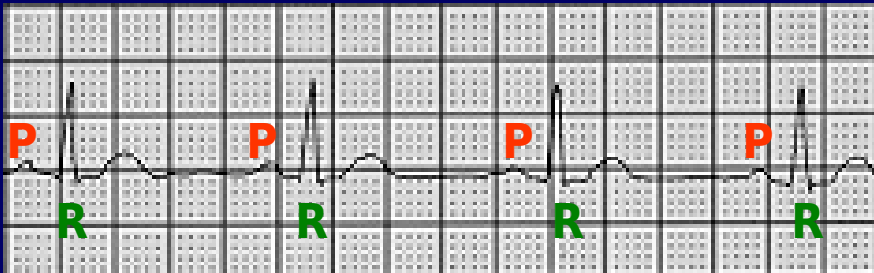
5. Day SC, et al. *Am J of Med.* 1982; 78:15-23.



The problem can originate in the sinus node ..



...or in the conduction system



There can be several causes of the symptoms

▣ Cardiac

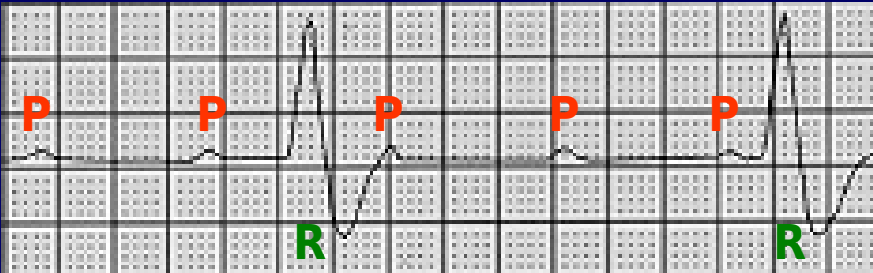
- Structural heart diseases
 - Obstruction to flow
 - Pump Failure
 - Cardiac Tamponade
 - Aortic dissection
- Arrhythmias
 - Bradyarrhythmias
 - Tachyarrhythmias

▣ Non-cardiac

- Reflex mechanisms
- Orthostatic hypotension
- Psychogenic

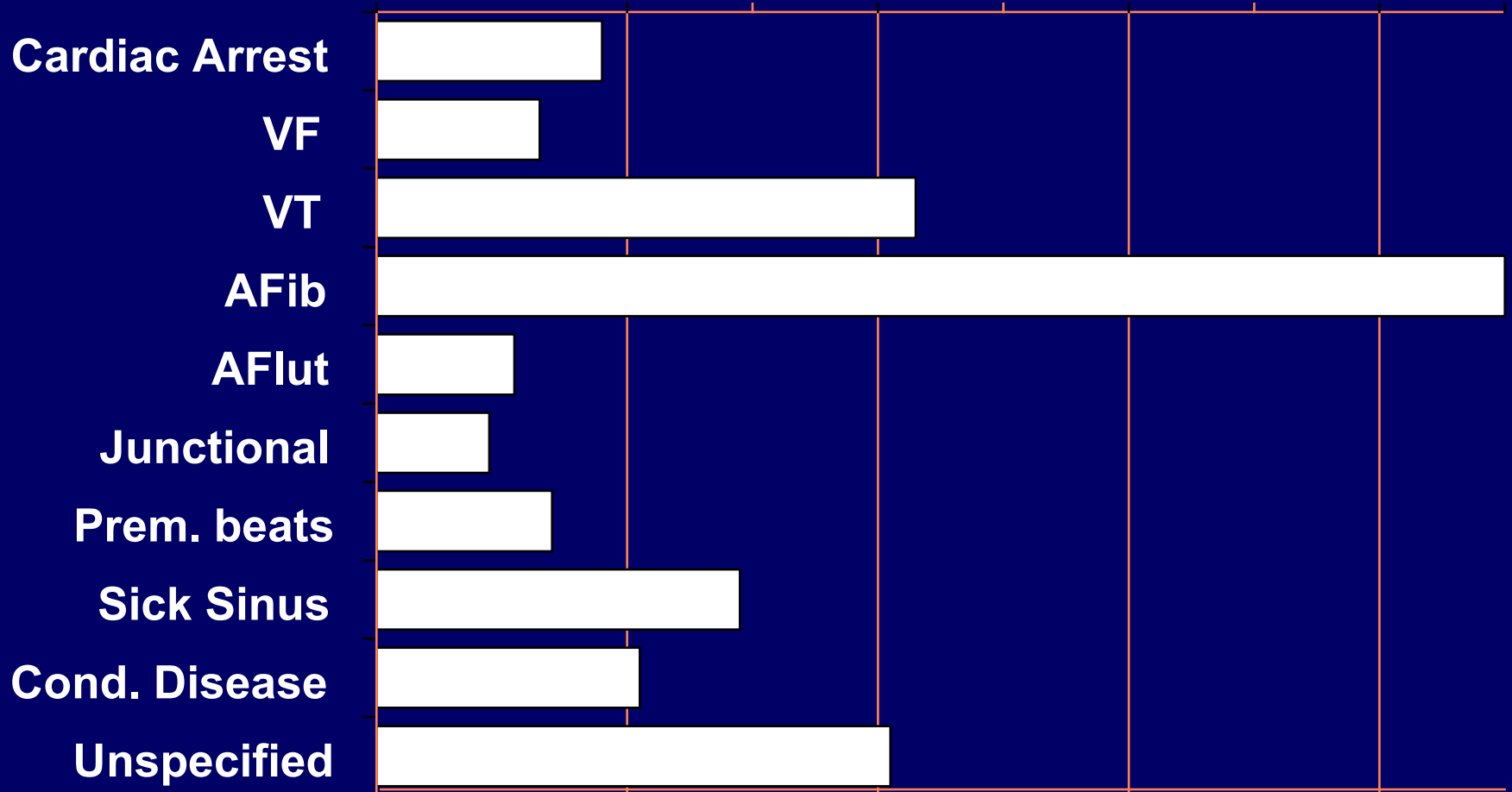


Goal: Document correlation of symptoms to the arrhythmia



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Arrhythmia Hospitalisation



The clinician has various tools to diagnose cardiac arrhythmias

- Patient history
- Physical exam
- 12-lead ECG
- Holter monitor
- Event recorder
- EP tests
- Implantable Loop Recorder - **Reveal +**



What is the Implantable Loop Recorder (ILR)?

- Useful for patients with infrequent symptoms who remain undiagnosed after the initial work-up
- Minimally invasive, leadless cardiac event recorder
- Provides up to 14 months of continuous monitoring
- Stores up to 42 minutes of ECG



Medtronic

Patient Selection Criteria

- ▣ Patients who experience transient symptoms such as difficult-to-diagnose syncope
 - Symptoms are infrequent
 - Symptoms are recurrent
 - Symptoms are unexplained



Why the ILR ?

- ▣ The less frequent the symptoms are...
 - The less likely conventional monitors will yield a diagnosis
 - The more testing you'll do
 - The more costly your attempt to diagnose becomes
 - The more frustrated the patient and physician become
- ▣ **Reveal[®] ILR may break the cycle of diagnostic testing**



Syncope Diagnosis

- Diagnostic “Gold Standard”¹
 - An ECG strip recorded during a spontaneous syncopal episode, i.e., symptom-rhythm correlation
 - Non-presumptive diagnosis of arrhythmic cause, or
 - Definitive rule-out of arrhythmic cause



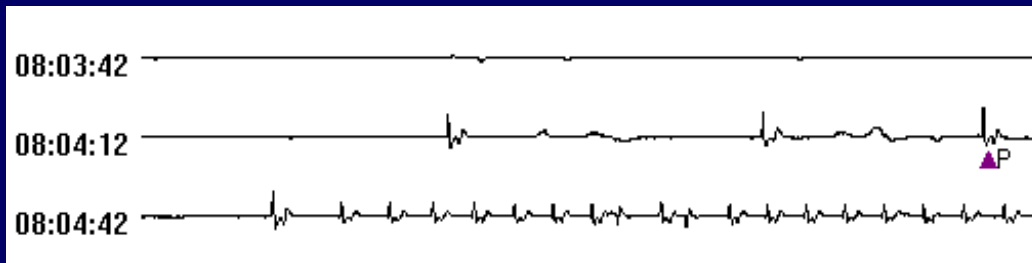
¹ Klein GJ, et al. *Circulation* 1995; 92:1332-1335.



Seizures & Syncope: A Case Example

After 15 years of having treatment-resistant epilepsy, a man received a Reveal[®] implant¹

Following a seizure, the Reveal showed a 36 second pause



After receiving a pacemaker, the episodes stopped



**If a correlation is found
between symptoms and ECG
changes..**



Medtronic

Is there a Bradycardia or a Tachycardia ?

- Is the cause reversible ?
- Will drug therapy affect the cause ?
- If the patient needs pacing.....
 - temporary or permanent ?



Temporary pacemaker



- Lead (s) connect the pacemaker to the cardiac chamber(s)

If the patient needs a Permanent Pacemaker...

What does a pacemaker do?

If the patient needs a Permanent Pacemaker...

It acts as a *replacement* for that part of the conduction system that is not functioning appropriately.

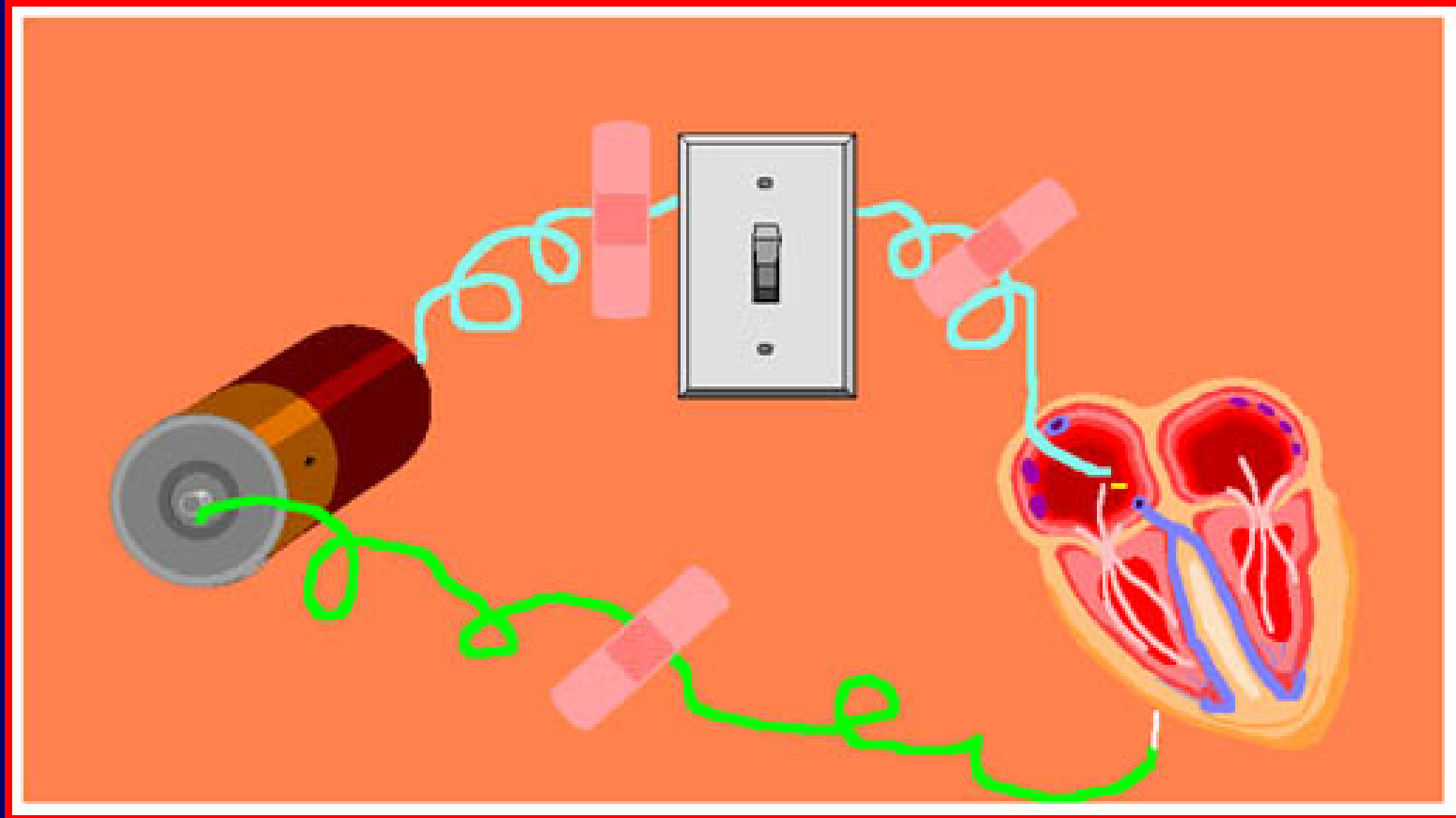


Medtronic

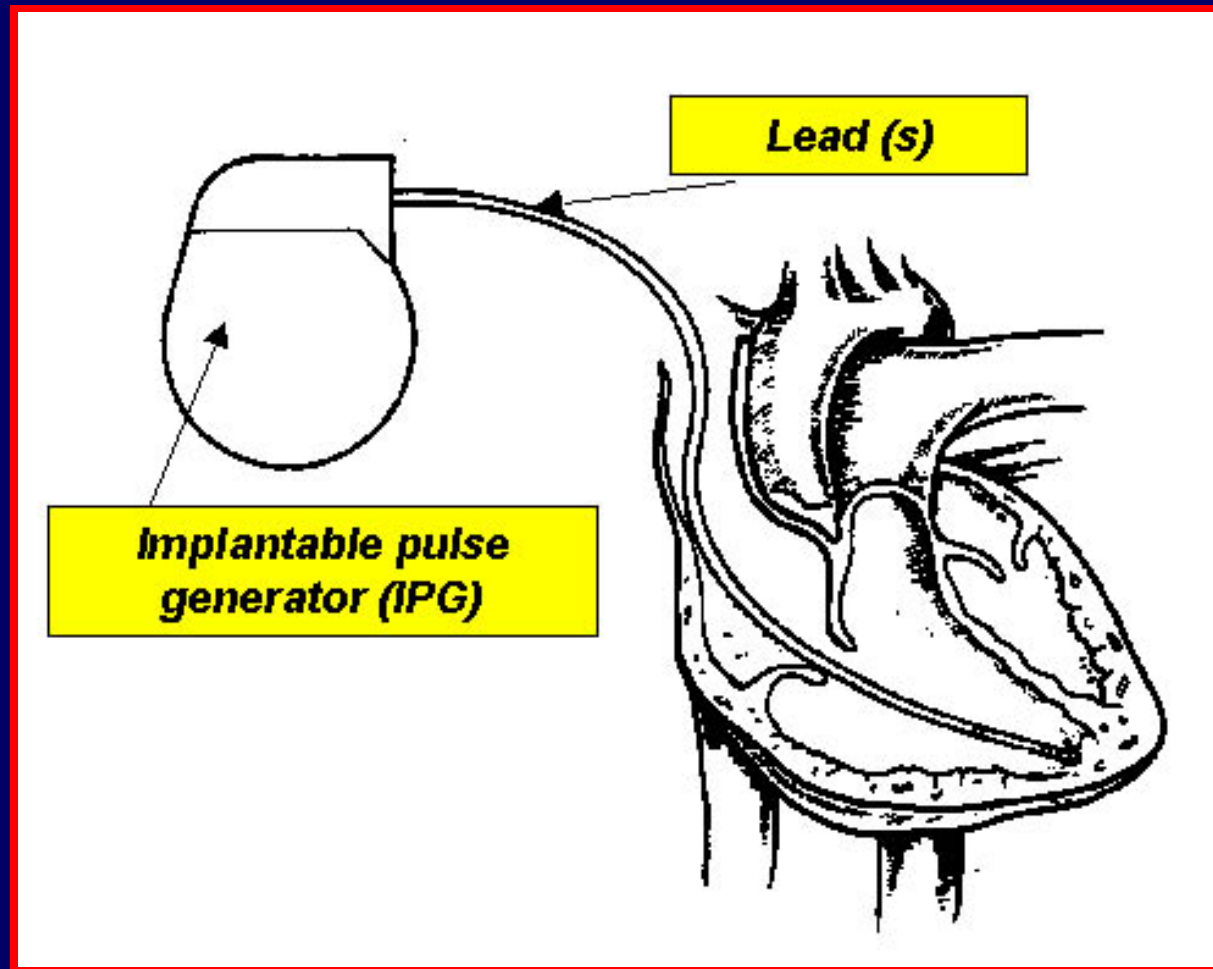
What is a Permanent Pacemaker?

A Pacemaker System consists of a
Pulse Generator plus Lead (s)

What is a Pacemaker?

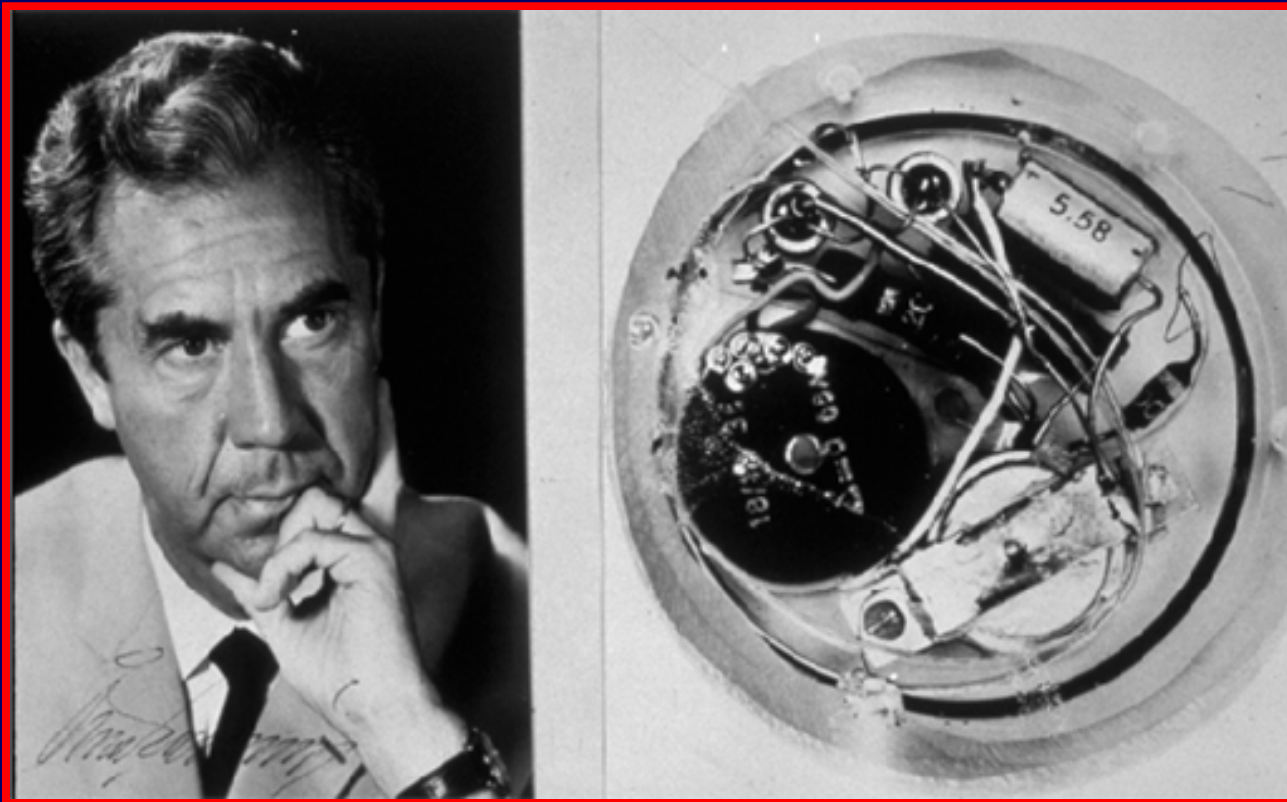


Relationship of the Pulse Generator & Lead



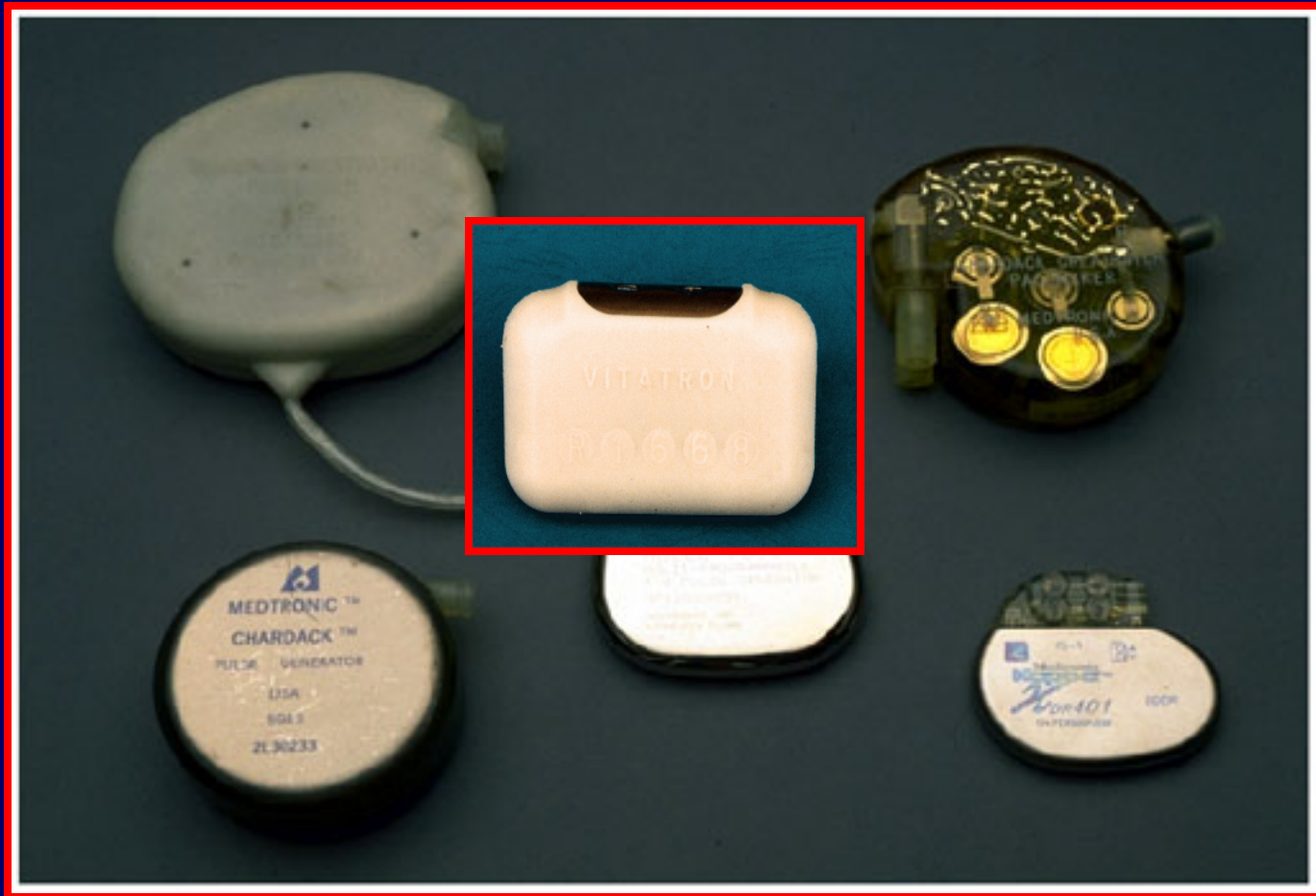
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What is a Pacemaker?

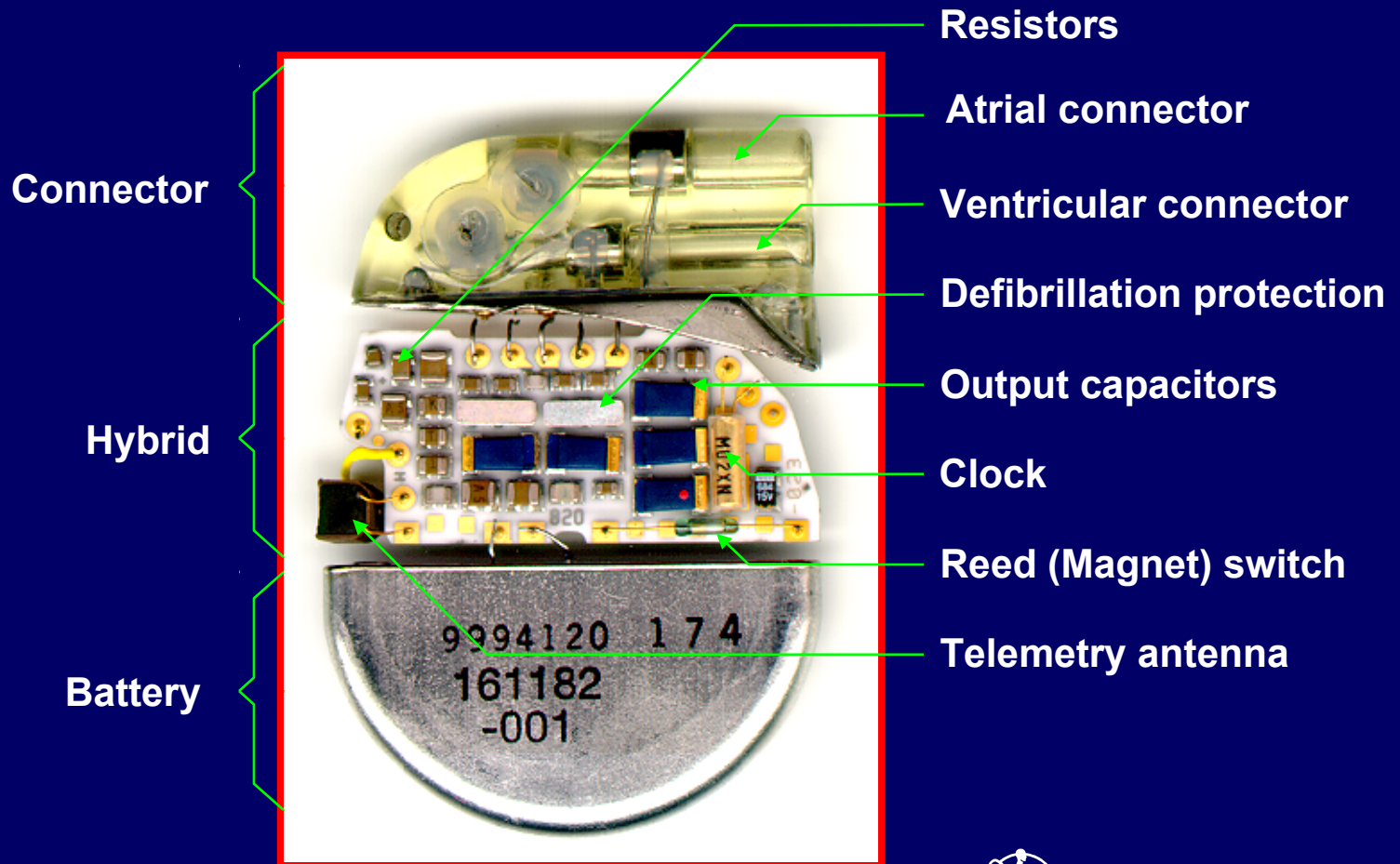


Medtronic

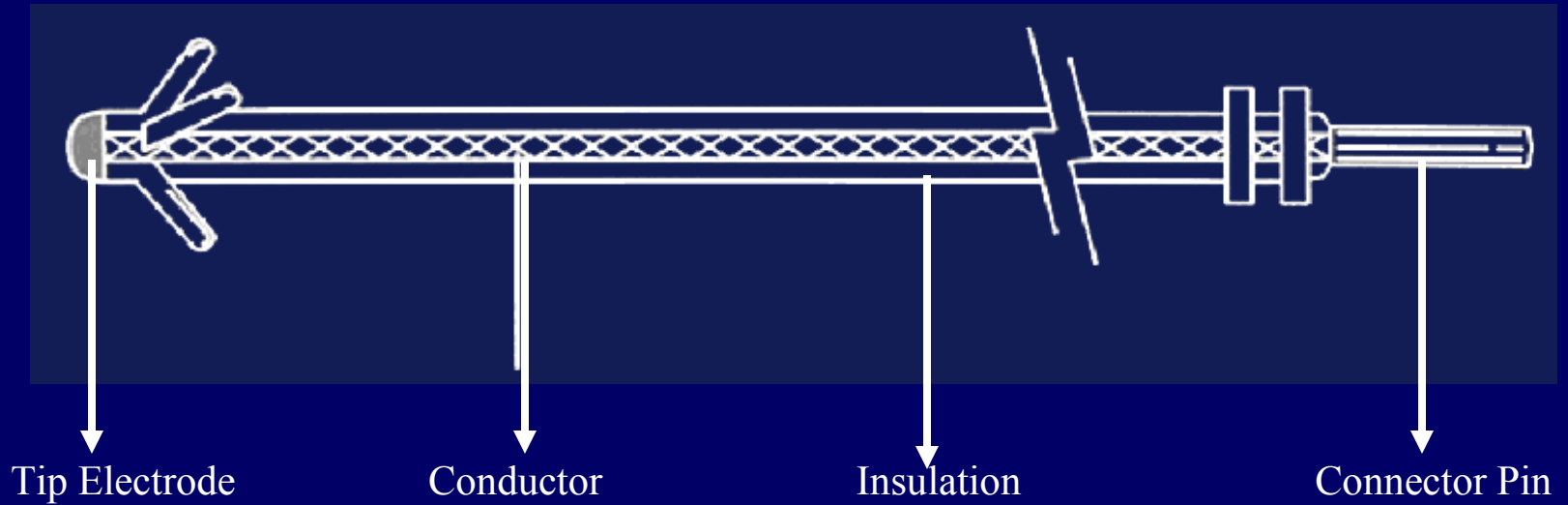
What is a Pacemaker?



Anatomy of a Pacemaker

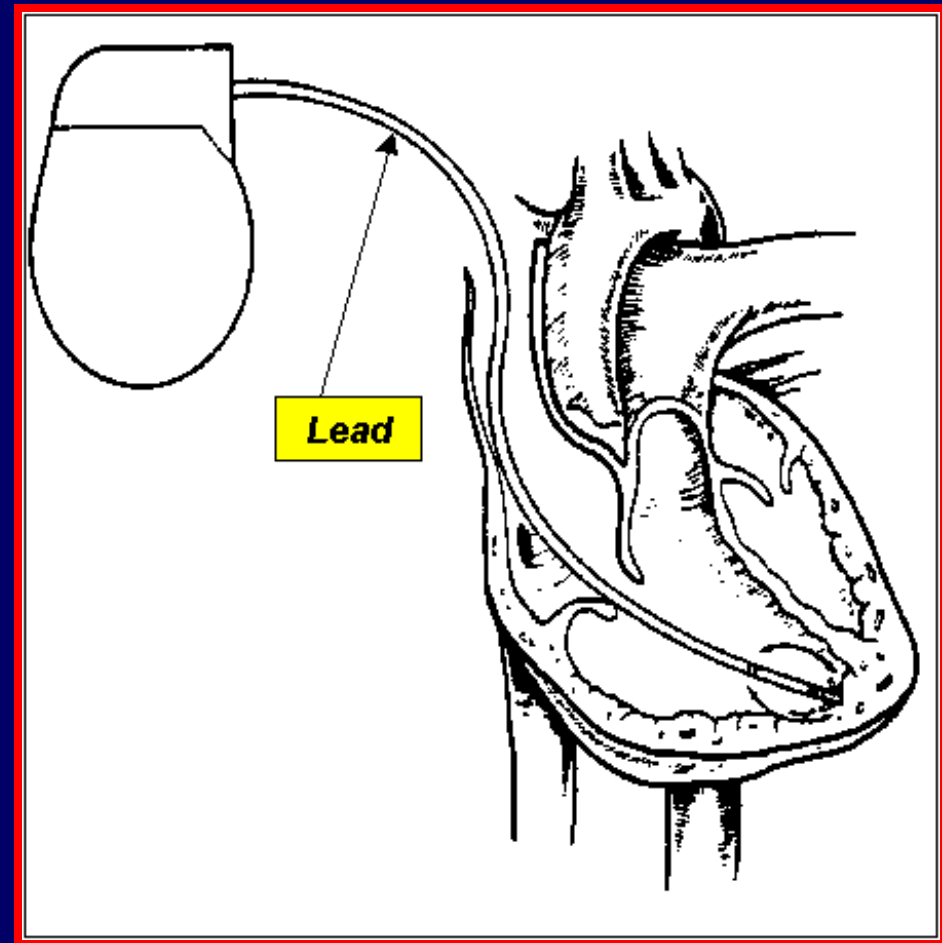


What is a Lead?

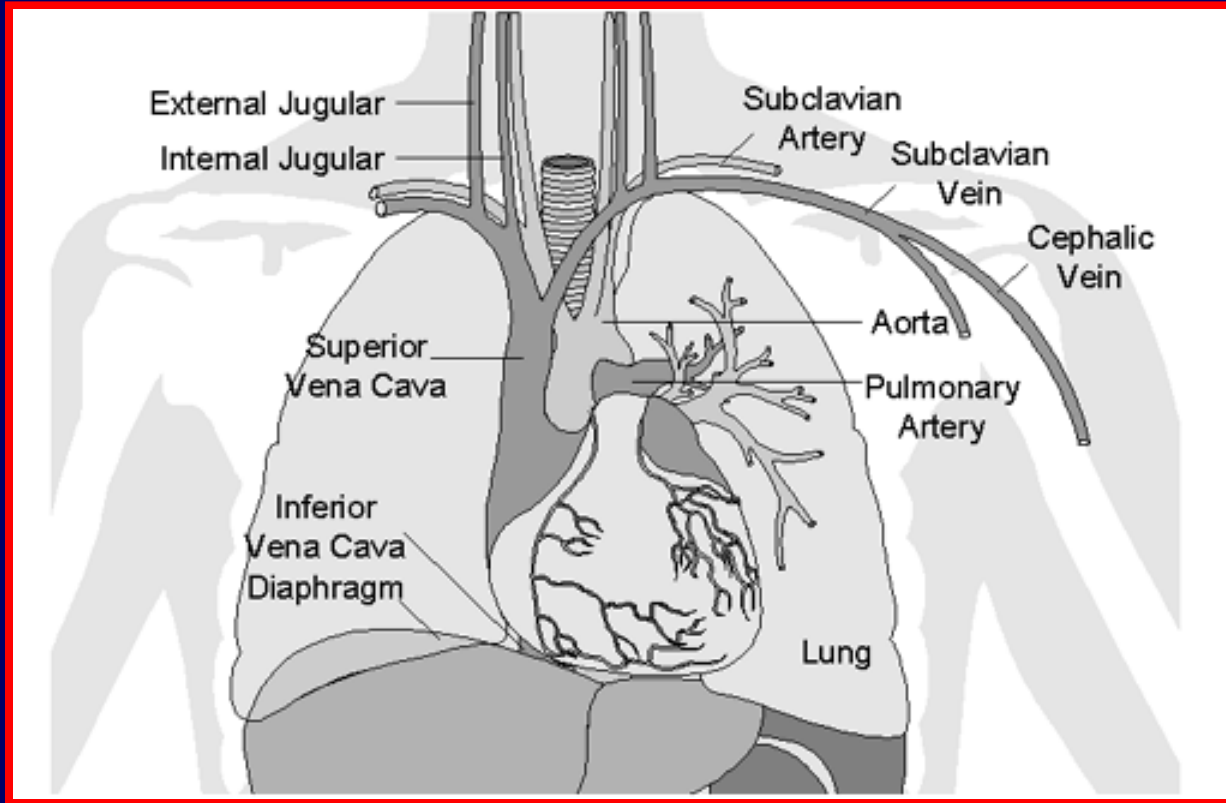


Leads Are Insulated Wires That:

- Deliver electrical impulses from the pulse generator to the heart
- Sense cardiac depolarisations

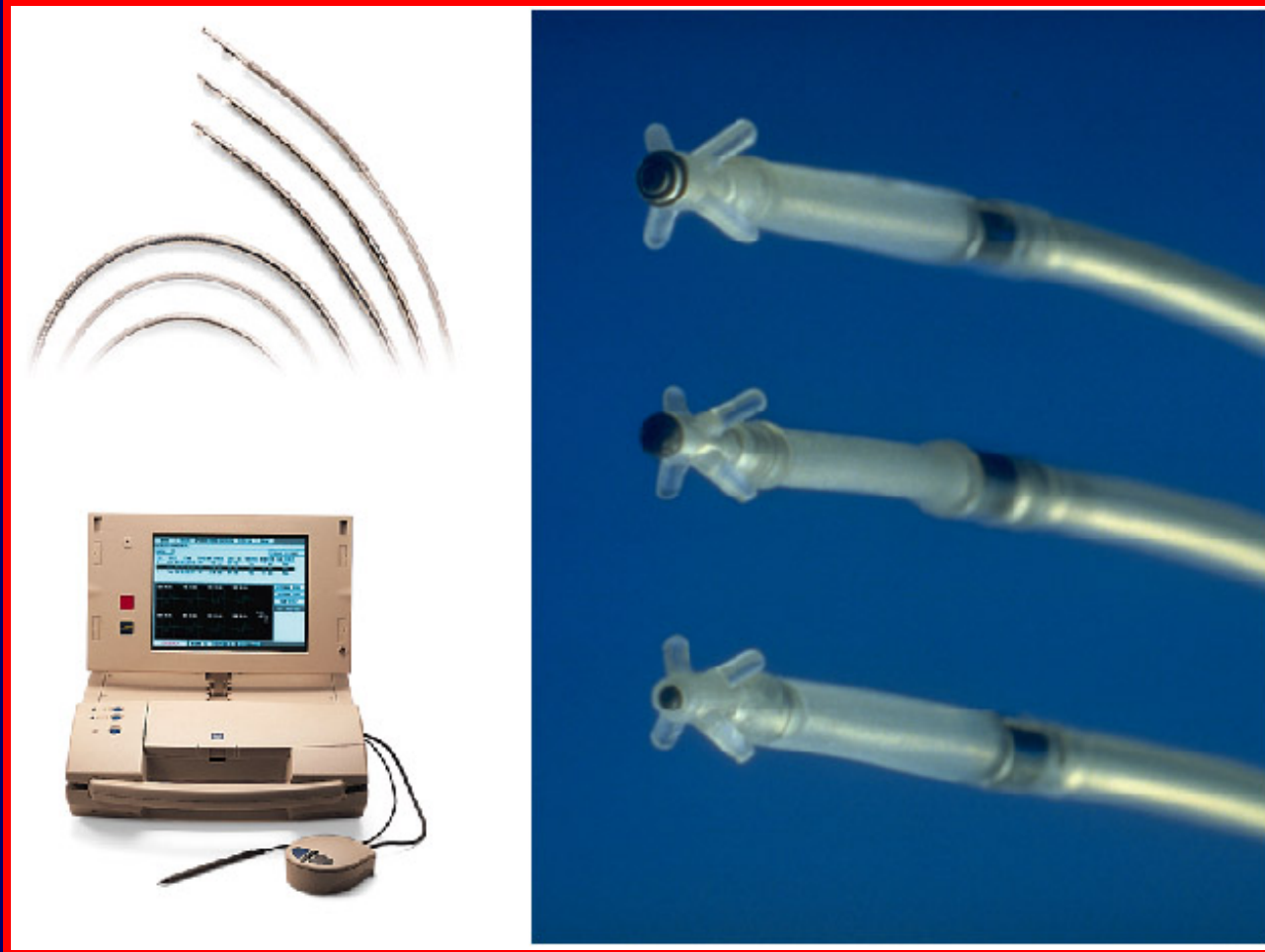


Leads are passed into the heart via veins:



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Bradycardia Pacing Products



CapSure,
CapSure SP,
and CapSure Z

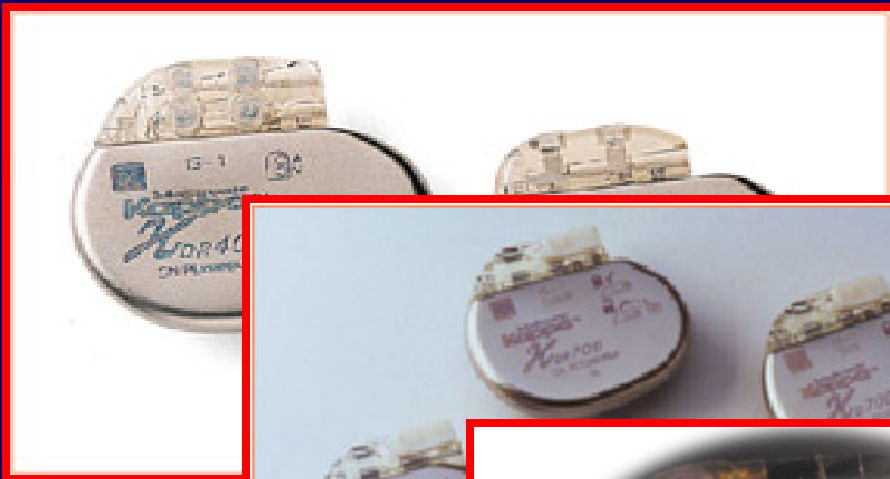
Bradycardia Pacing Products



CapSure Z and CapSureFix Pacing Leads

Bradycardia Pacing Products

Medtronic.Kappa Series



**Medtronic.Kappa 400
Dual Sensor Pacemakers**



**Medtronic.Kappa 700
Automatic Family
of Pacemakers**



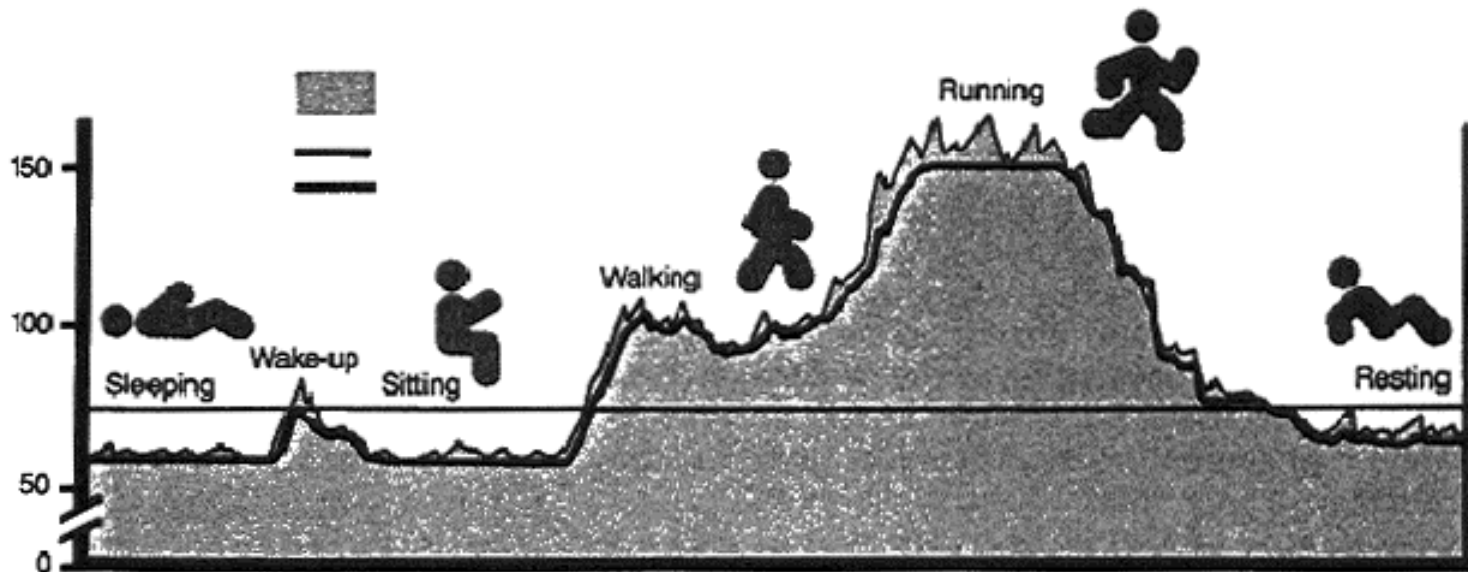
**Medtronic.Kappa 900
Automatic Family
of Pacemakers**



Medtronic

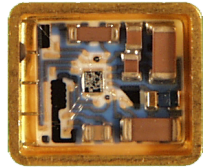
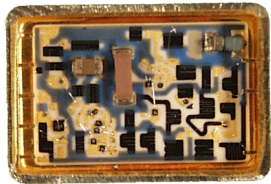
Rate Responsive Pacing

- When the need for oxygenated blood increases, the pacemaker ensures that the heart rate increases to provide additional cardiac output



Medtronic

25 Years of Technology Growth



1975

Xyrel

**Fixed Rate,
Synchronous
Pacing**

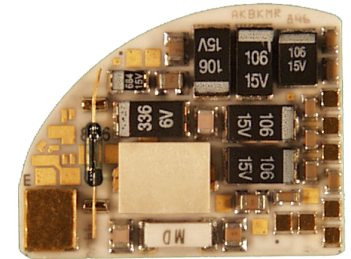
Transistor Count: 35

User's Manual 20 pages

*No Programming
Available*

Kappa 700

**Fully programmable,
physiologic pacing,
extensive diagnostics**



1998

Transistor Count: 900,000

User's Manual 670 pages

*No Programming
Necessary*

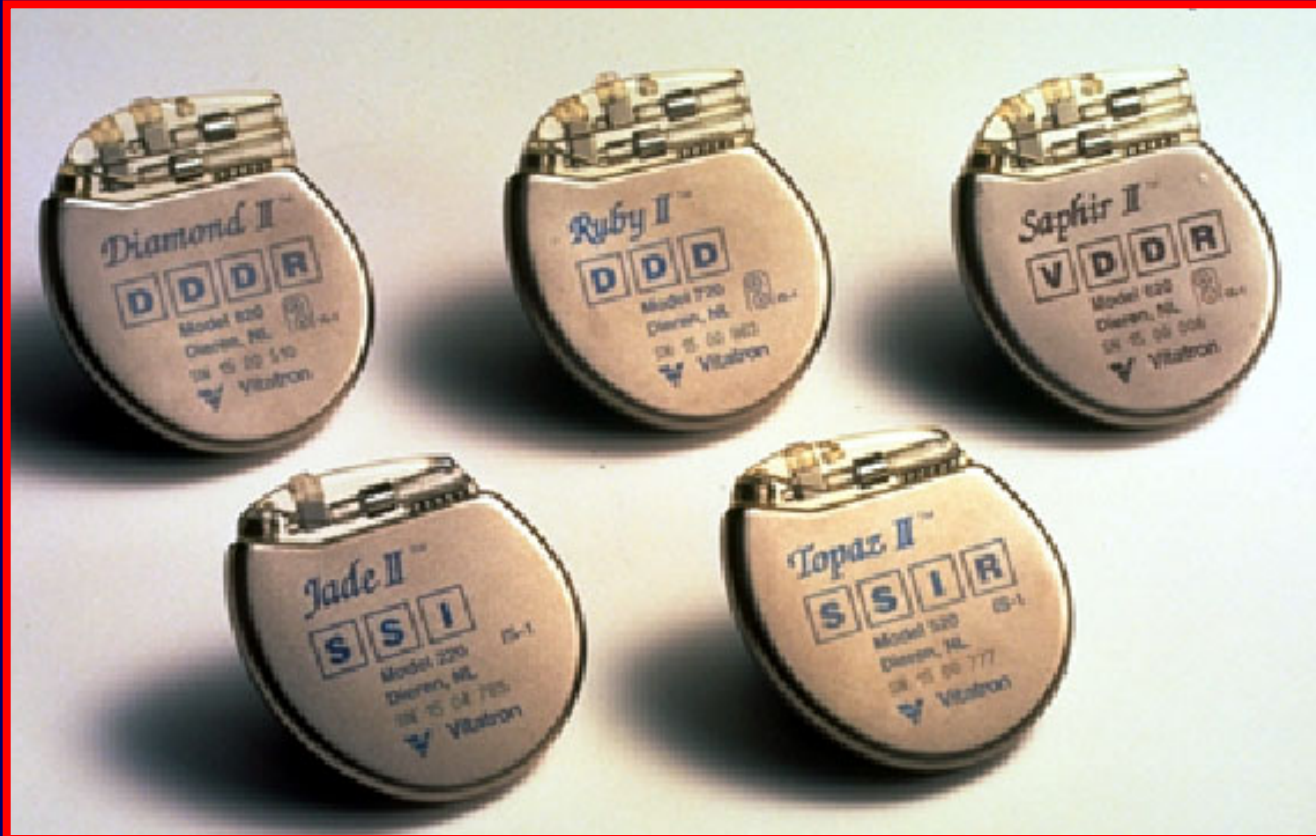


**Xyrel in 1998
Technology**



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Vitatron Products



Medtronic

DA+: World's First Digital Pacemaker

First clinical implant of the new vitatron C-series pacemaker worldwide

Arnhem, The Netherlands, 31 January, 2003 –

Today, Vitatron announced the start of an international multi-center clinical device study evaluating its new Vitatron C-series: the first fully digital pacemaker in the world. The first implant took place at the University Clinic in Graz, Austria, by Professor Dr. K.H. Tscheliessnigg and his team.

vitatron

**How do we know what a
pacemaker has been doing?**

How do we know what a pacemaker has been doing?

Traditionally, the patient comes to a pacing clinic...

The pacemaker is interrogated using a Programmer



Medtronic

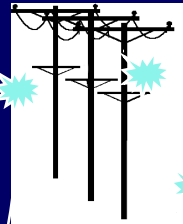
But with Remote View..



The customer requests help from the remote consultant/MDT



The consultant/MDT, via their PC, calls the CareLink Programmer



A Remote Session

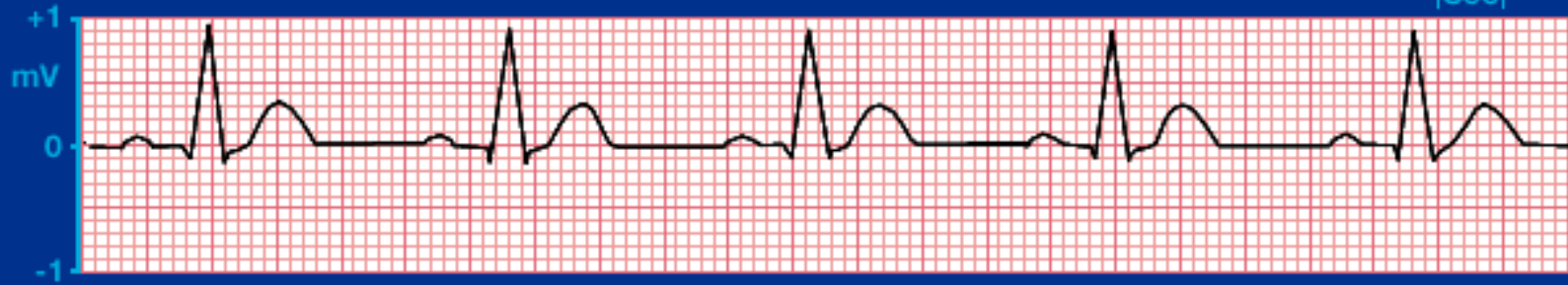


Medtronic

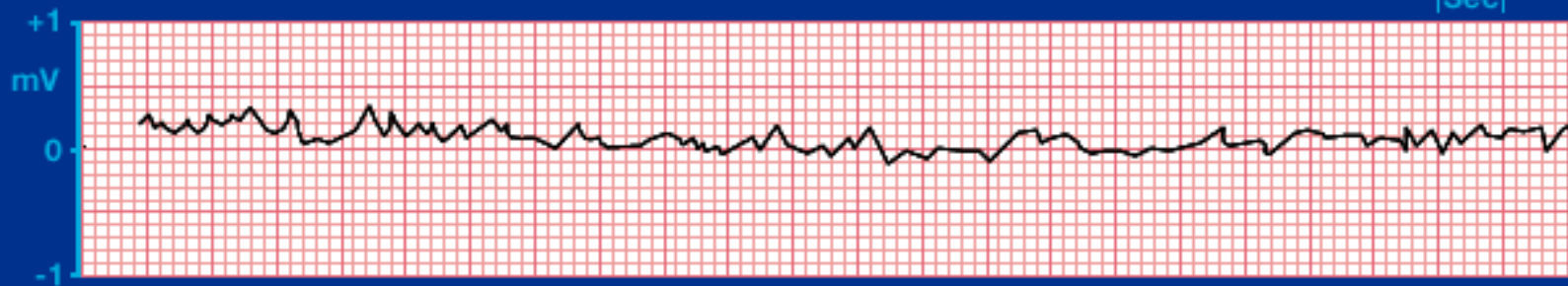
Tachyarrhythmia Management

NSR and VF

Normal Sinus Rhythm



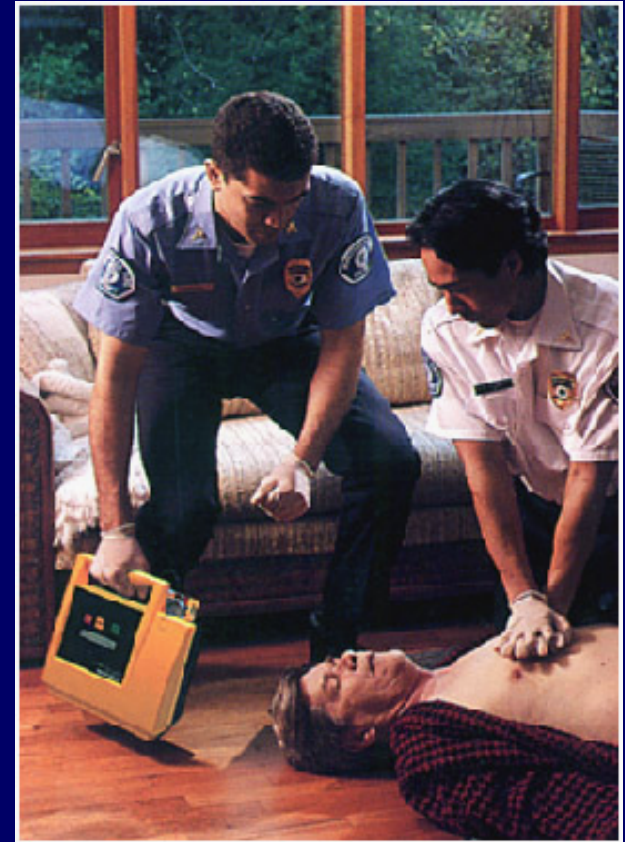
Ventricular Fibrillation



Physio-Control

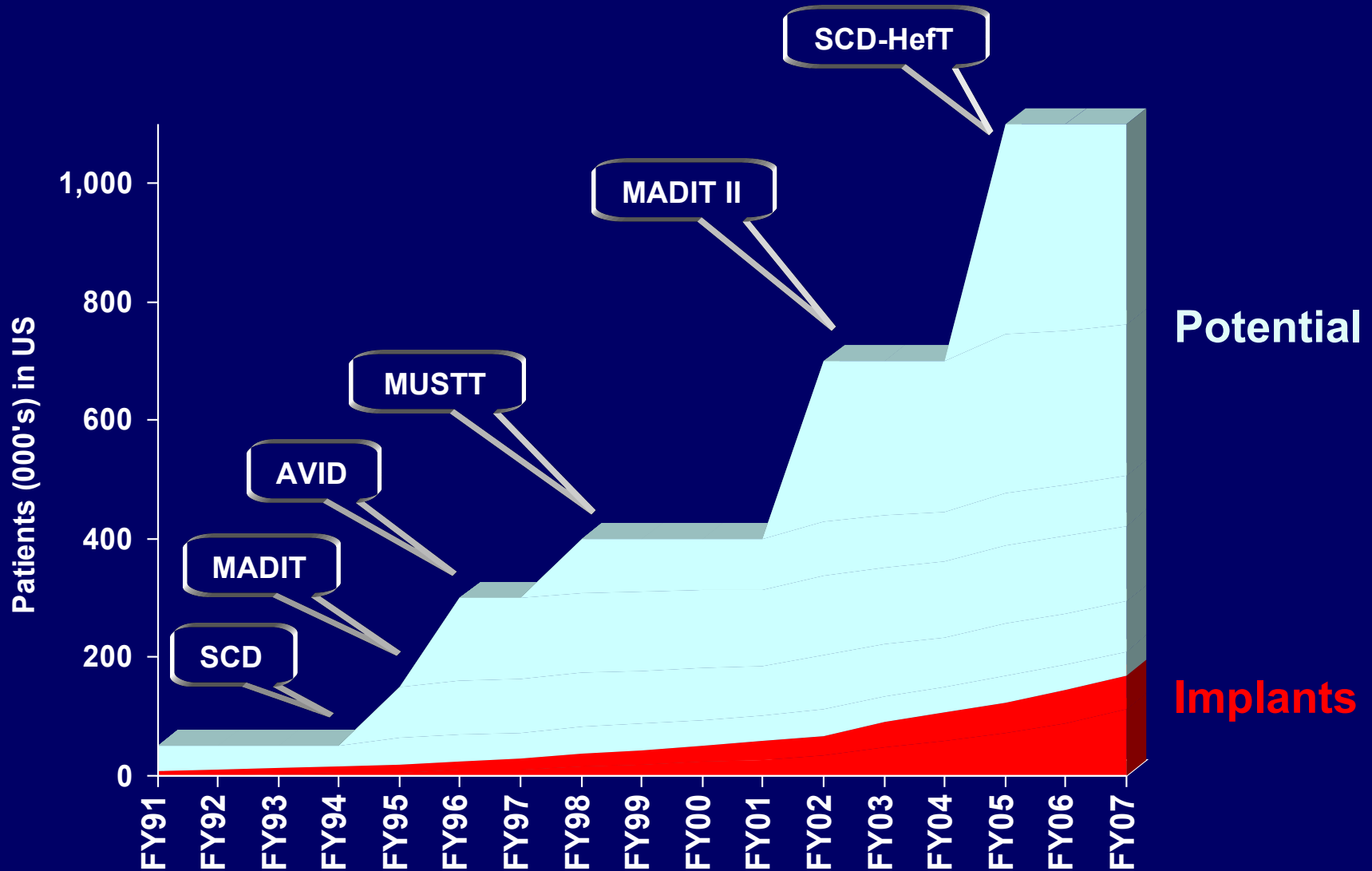
Today:

- ▮ **Sudden Cardiac Death is the most common cause of death in the U.S.**
- ▮ **Sudden Cardiac Arrests in the U.S. annually: 400,000**
- ▮ **Less than 5% survive**



Medtronic

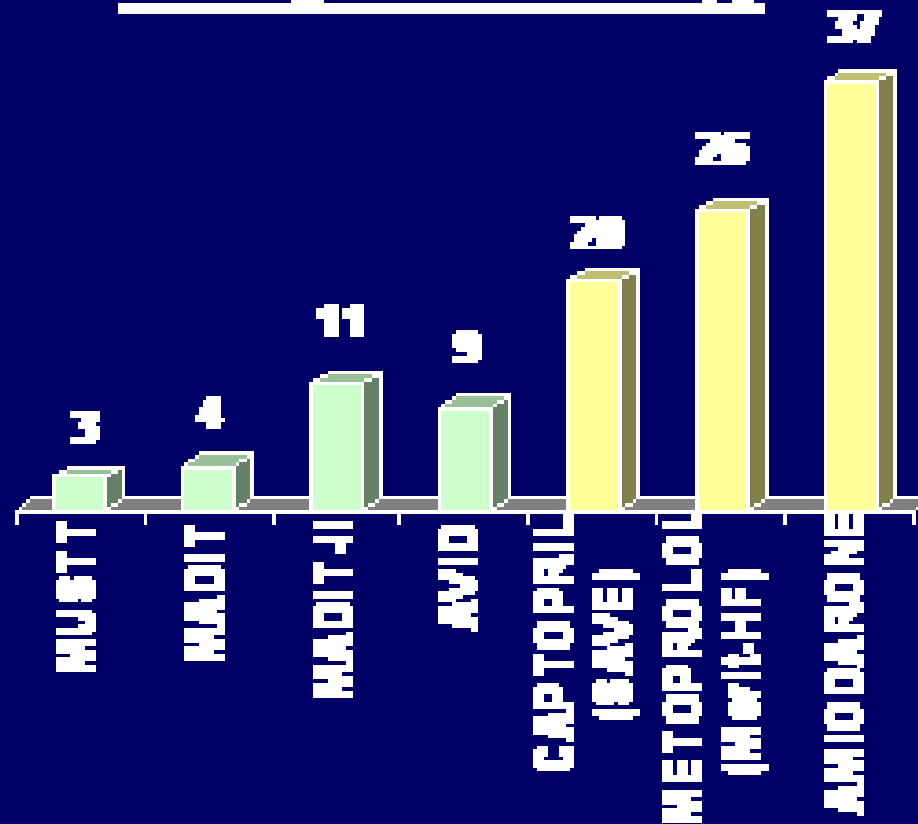
ICD Implant Potential



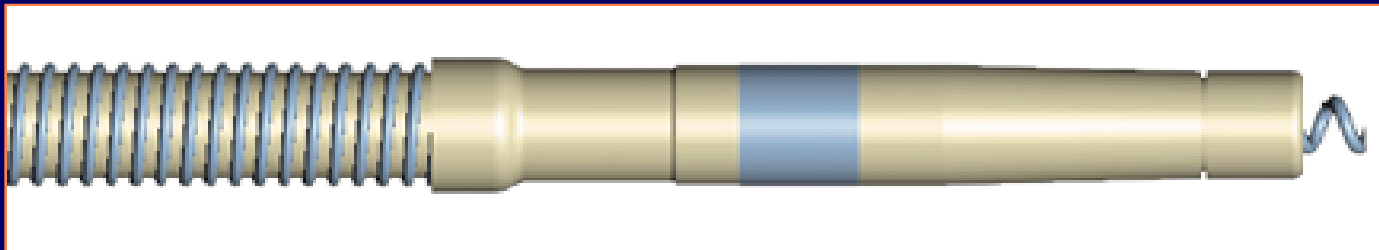
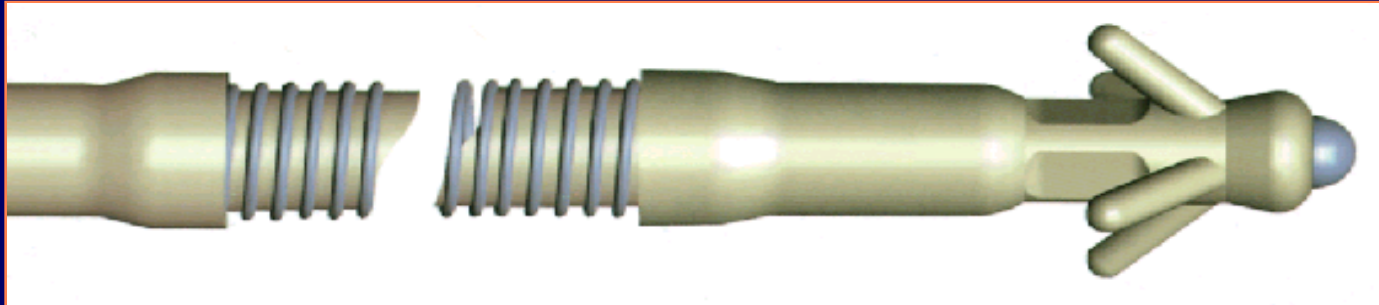
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ICDs are more effective than drugs

Number Needed to Treat to Save One Life Select CV Drugs vs. ICD Therapy

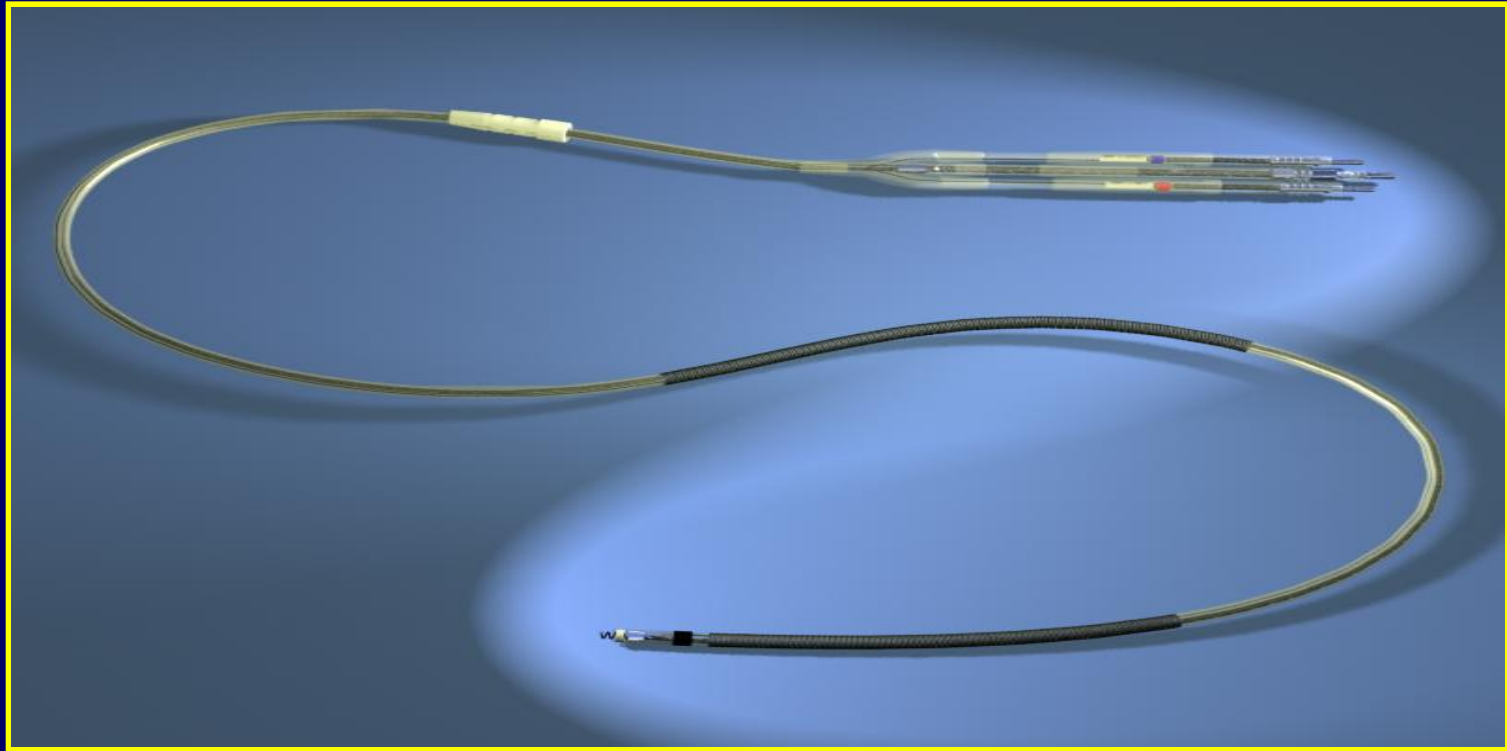


Defibrillation Systems Products



Leads

Defibrillation Systems Products

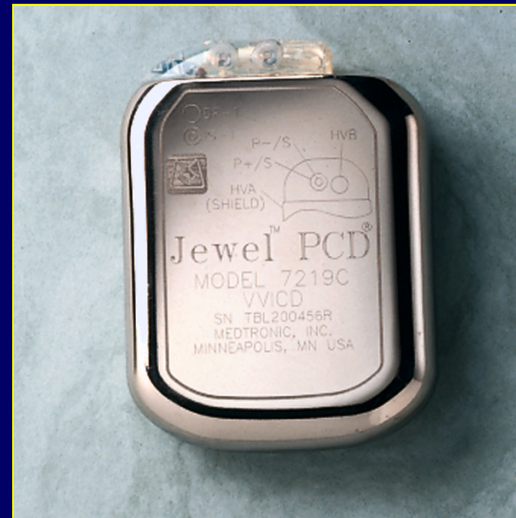


6947

A Decade of Change in ICD Technology



- ❖ 1989 - Model 7216A
- ❖ 209 cc; 281 g
- ❖ 34 Joule output
- ❖ ATP



- ❖ 1993 - Model 7219C
- ❖ 80 cc; 129 g
- ❖ 34 Joule output
- ❖ Active Can®



- ❖ 1996 - Model 7223Cx
- ❖ 54 cc; 97 g
- ❖ 30 Joule output
- ❖ EGM-width



Medtronic

The World's Most Advanced Full-Featured Implantable Defibrillator

- ❖ 2001 – Marquis DR
- ❖ 36 cc; 75 g
- ❖ 30 Joule output
- ❖ painless lead impedance
- ❖ patient alert
- ❖ rate responsive pacing
- ❖ advanced detection criteria
- ❖ Automatic P- and R-wave measurements
- ❖ Cardiac compass



Medtronic

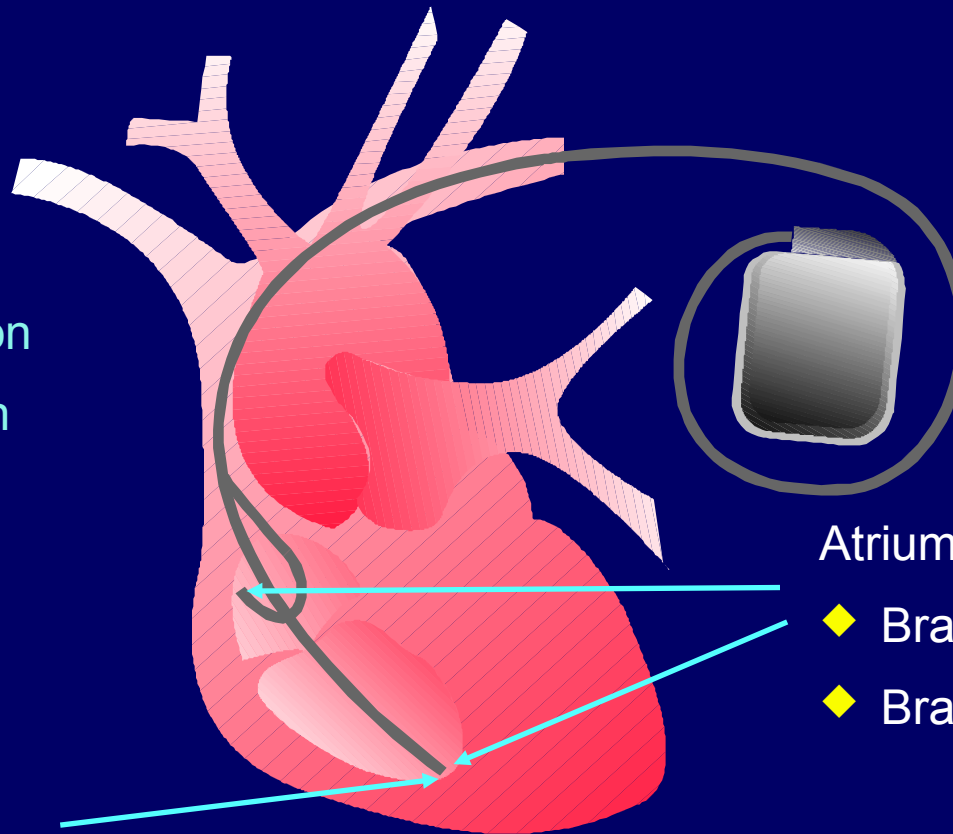
Therapies Provided by Today's Dual-Chamber ICD's

Atrium

- ◆ ATP
- ◆ Low-energy cardioversion
- ◆ Defibrillation

Ventricle

- ◆ ATP
- ◆ Low-energy cardioversion
- ◆ Defibrillation



Atrium & Ventricle

- ◆ Bradycardia sensing
- ◆ Bradycardia pacing



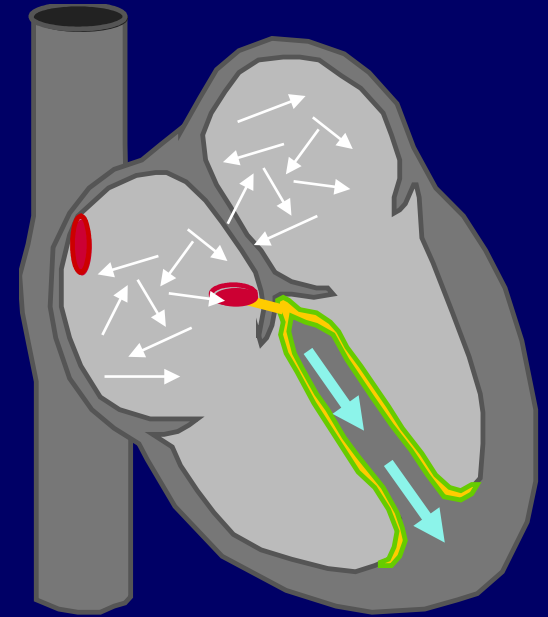
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Atrial Fibrillation

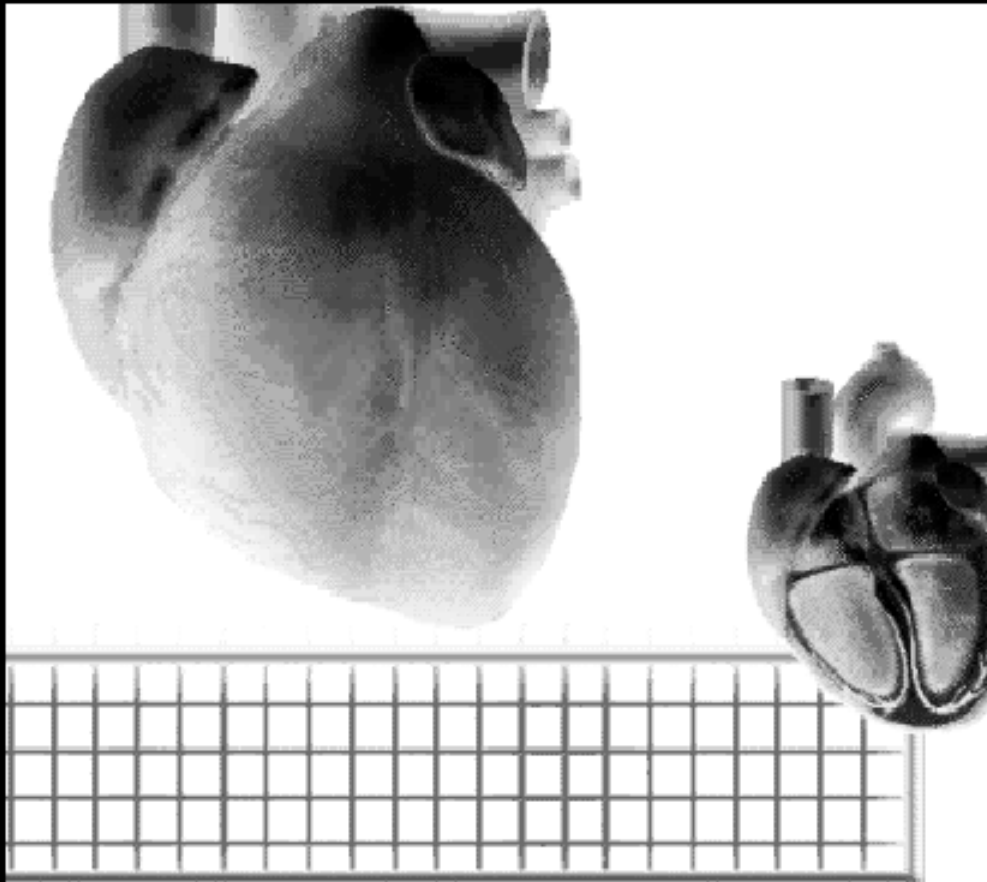
A Business Overview

What is Atrial Fibrillation

- First described in 17th century by Sir William Harvey¹
- James Mackenzie - 'pulsus irregularis perpetuus' in 1903
- Chaotic electrical activity in the atrium with irregular and fast ventricular response
- Most common sustained cardiac arrhythmia



Clinical Impact of Atrial Fibrillation

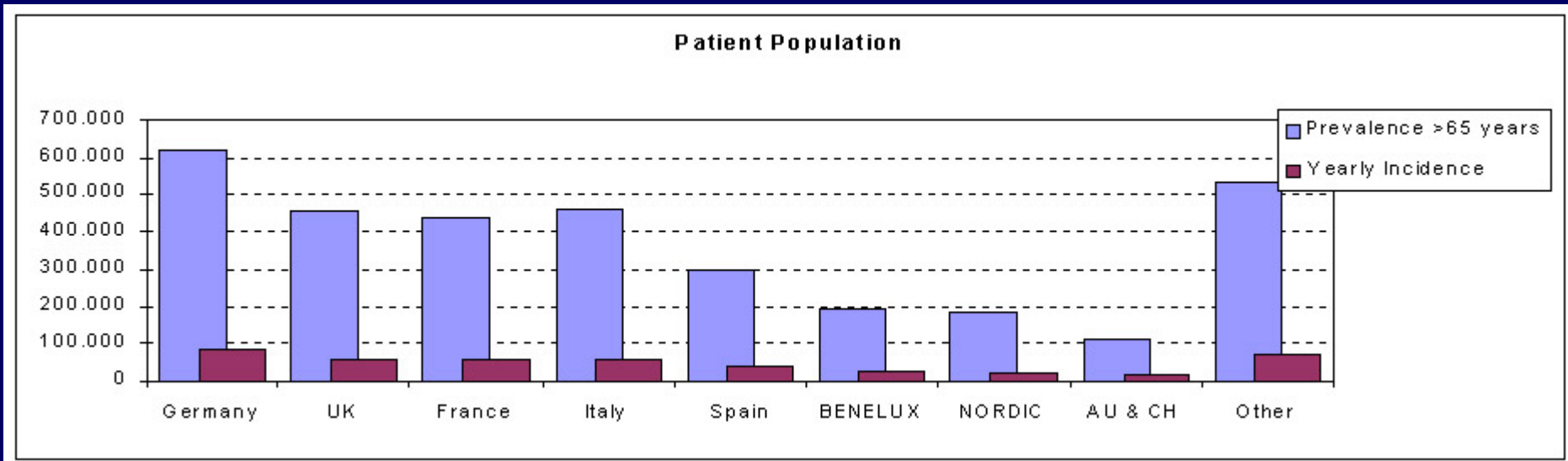


Stroke
CHF
Embolism
Palpitations
Dyspnea
Angina
Exercise intolerance
Fatigue
Vertigo



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Incidence & Prevalence of AF



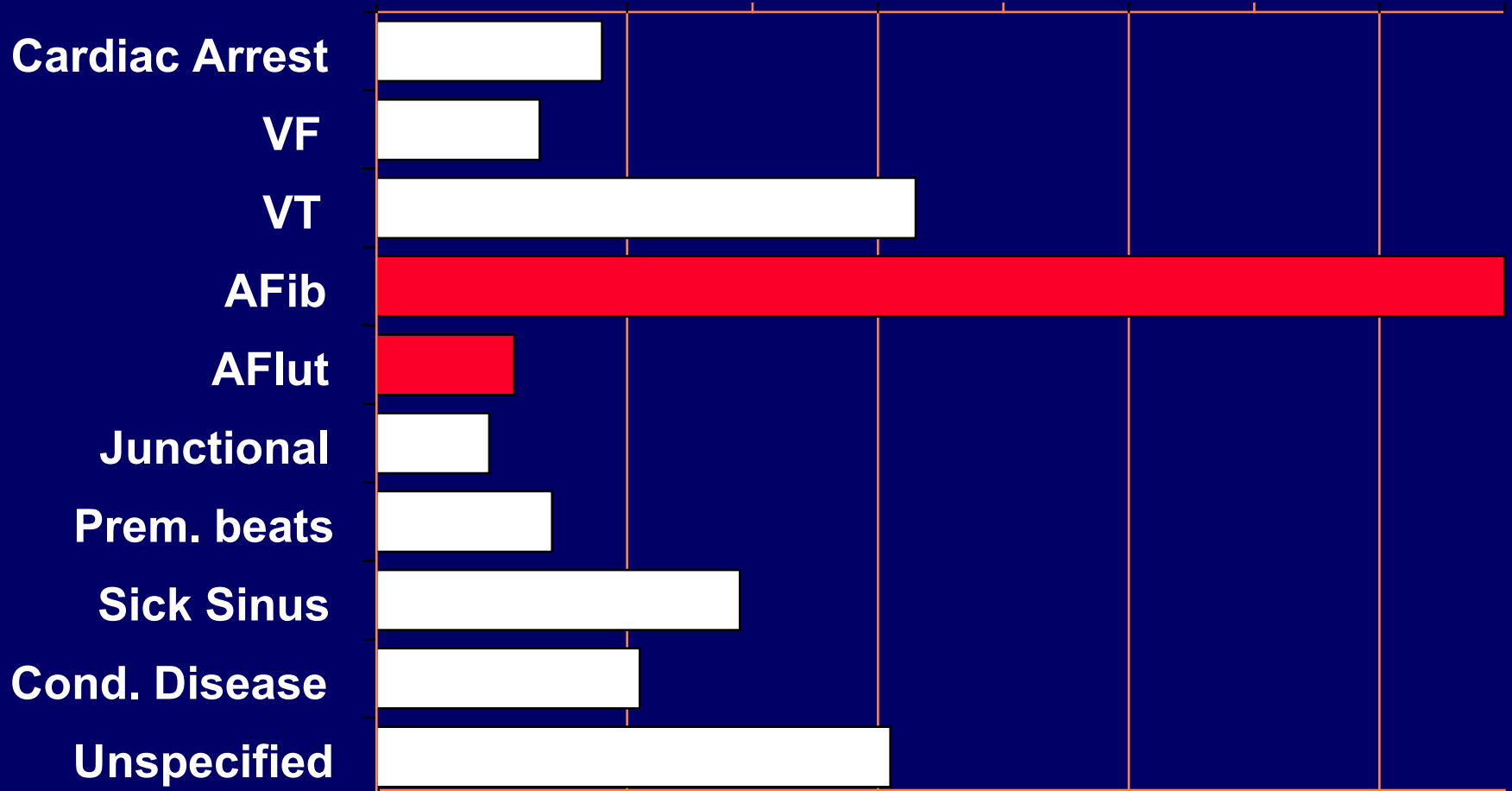
Ca. 3.3 Mio patient
suffer from AF
today

Ca. 432'000 new
AF patients each
year



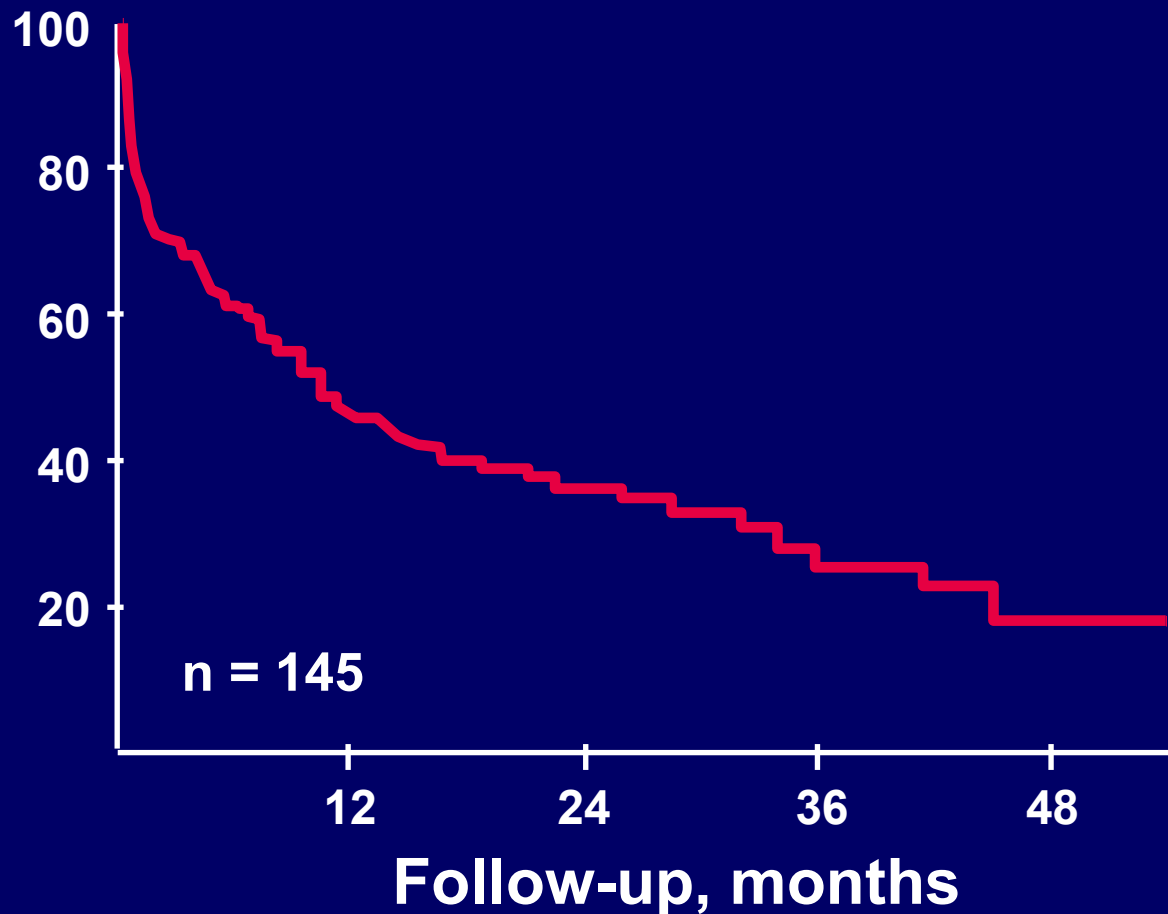
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Arrhythmia Hospitalisation



Antiarrhythmic Drug Treatment

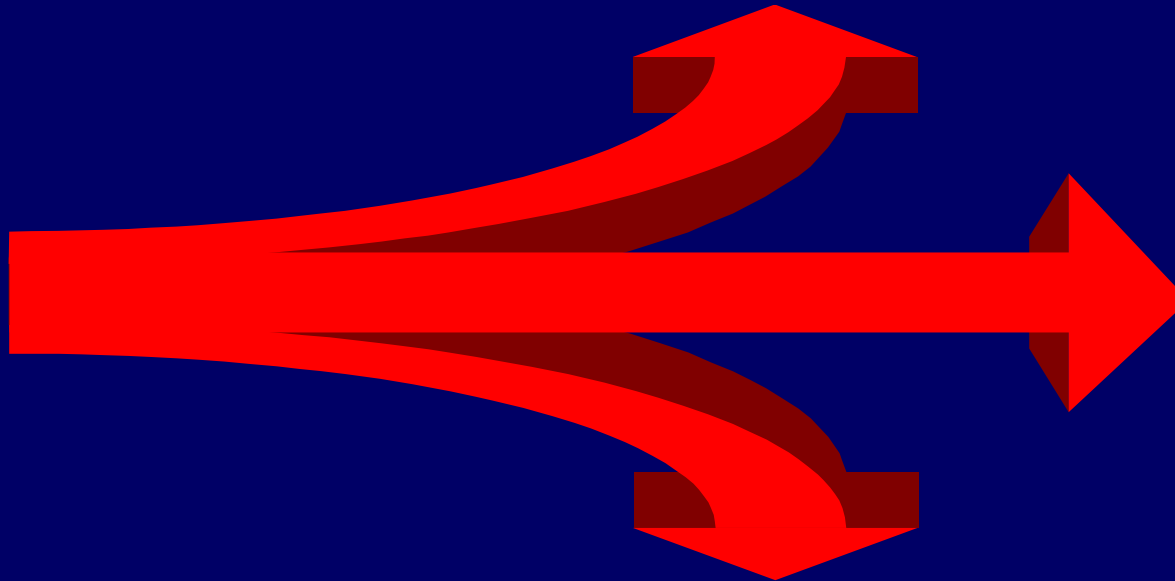
% Patients
free of AF
recurrence



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Product Strategy for Atrial Fibrillation

**High Energy Device
Model 7262**



**Low Energy Devices
AT500 & Selection**

**Ablation Tools
Amazr & Maze Pen**



Medtronic

Medtronic GEM III AT

Second generation high energy
atrial & ventricular
Arrhythmia Management Device



- ▣ Atrial prevention
- ▣ Atrial & ventricular pace therapies
- ▣ Atrial & ventricular shock termination
- ▣ 39 cc, 77 grams, 13.5 mm
- ▣ 30 Joules



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Medtronic AT500

First low-energy atrial Arrhythmia Management Device



- ▣ Extensive monitoring for atrial arrhythmias
- ▣ Arrhythmia prevention algorithms
- ▣ Atrial anti-tachy pacing & 50 Hz burst
- ▣ Dual-chamber, rate responsive pacing
- ▣ 15cc, less than 30g
- ▣ 5 years nominal longevity



Medtronic

Vitatron Products

DiagnoseAF

Dual Chamber DDDR Dual Sensor

- Beat-to-Beat ModeSwitching
- AF focused diagnostics
- Save-to-disk
-> AFdiscover

PreventAF



4 AF preventive pacing Algorithms:

- Pace Conditioning
- PAC Suppression
- Post PAC response
- Post Exercise Response

Selection 9000



Upgradeability: AF3.0



Fixed:
Selection 900E AF1.0



Fixed:
Selection 900E AF2.0



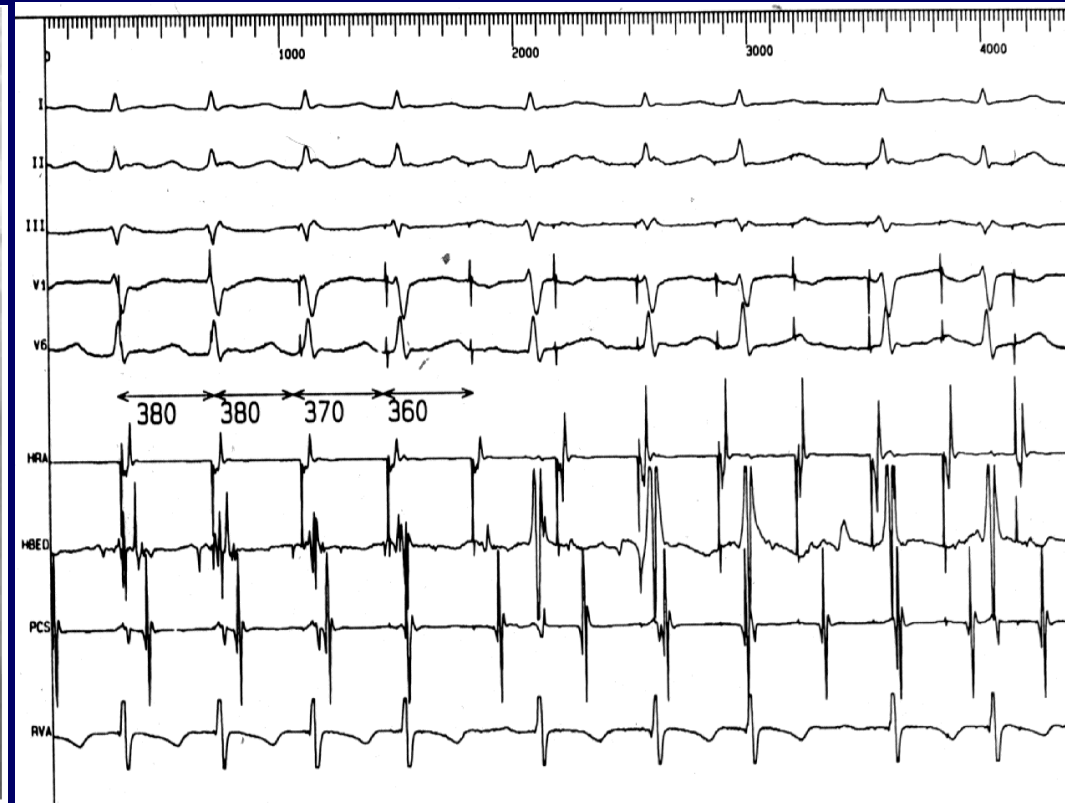
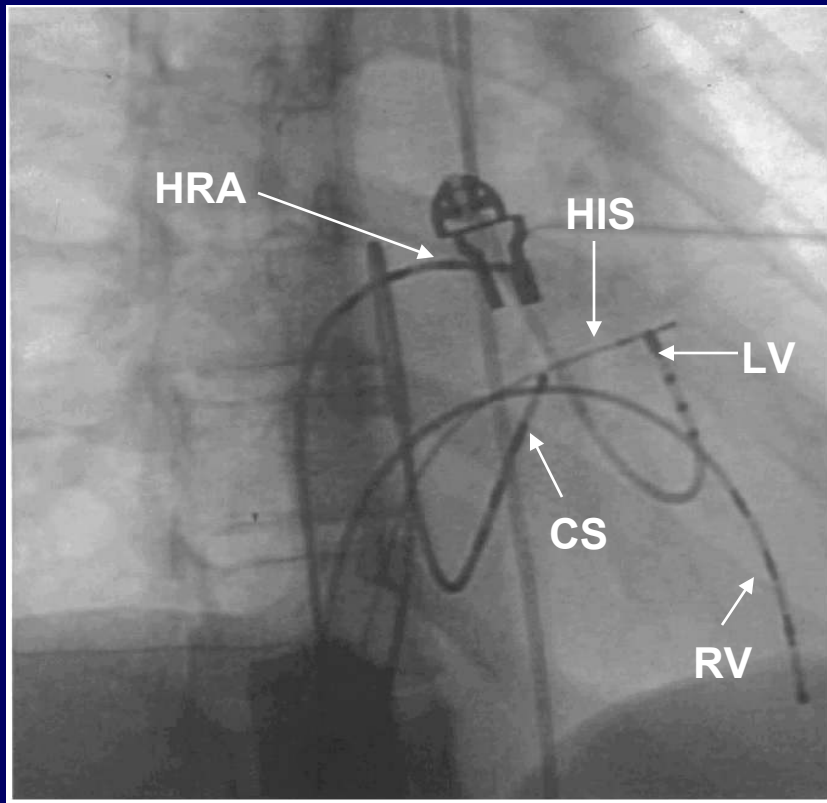
Upgradeable:
PreventAF



EP-Systems

- **Diagnostic catheters**
- **Radio Frequency (RF) Ablation catheters**
- **RF Generators**
- **Catheter Navigation Technology**





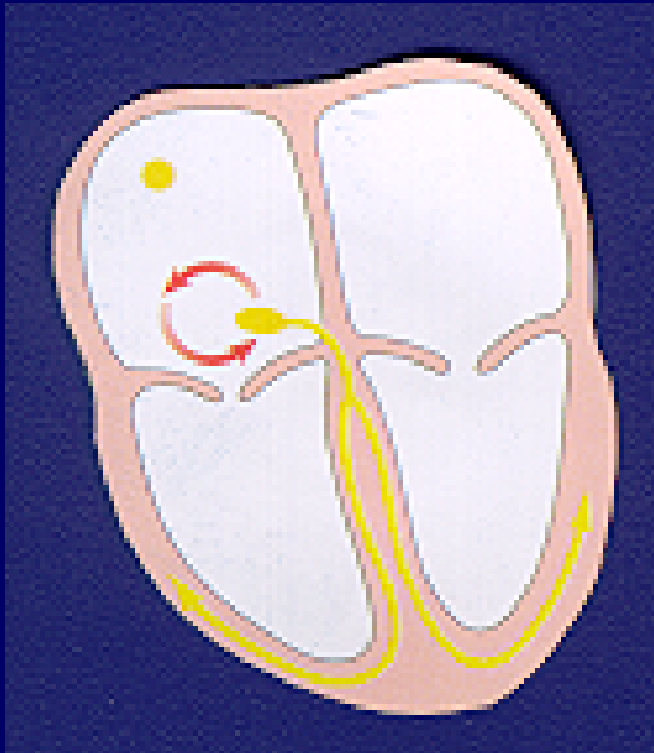
- Catheters in the heart allow to observe the ECG together with local intracardiac egm's from inside the heart.
- These recordings allow diagnosis of arrhythmias
- What is the mechanism? How does it work? Is the arrhythmia life threatening?
- What is the best treatment? Can we cure it by RF-ablation?
- Or ICD implant? Or?

RF Ablation

- ▮ **Destruction of a distinct area in the heart to interrupt the re-entry circuit or take out the focus of a tachycardia**
- ▮ **This is done by local heating with High Frequency energy (RF energy)**
- ▮ **Curative therapy: no more need for medication or implantable devices after successful treatment**
- ▮ **Effective for most tachycardias and expanding**



Arrhythmia Example



- **AV Nodal Re-entry Tachycardia (AVNRT)-**

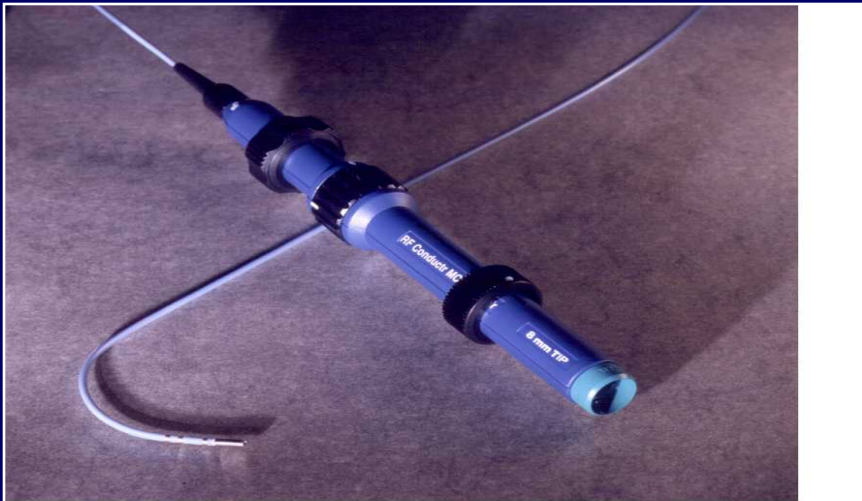
Most common form of SVT.

An extra pathway exists in or next to the AV node.



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RF Ablation Catheters



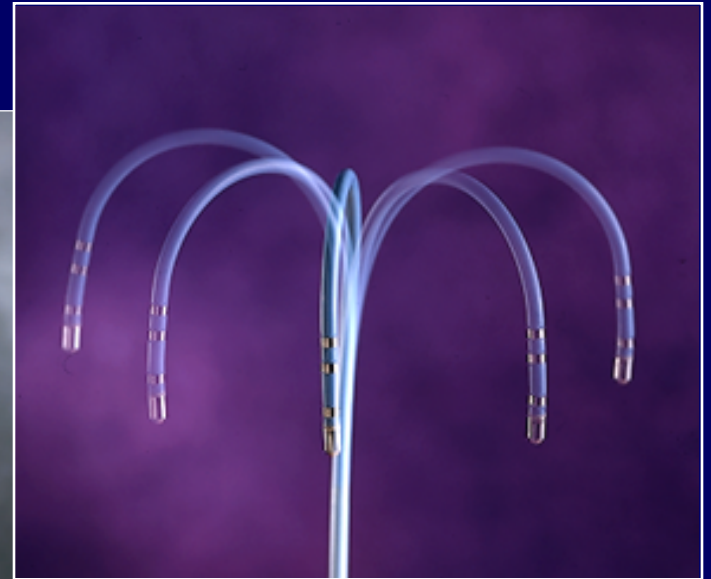
- ▣ Enhancr
 - steerable 7F
- ▣ Conductr
 - multi steerable 7F
- ▣ Marinr 5F
 - pediatric & geriatric
- ▣ Contactr
 - Atrial Flutter
- ▣ Amazr
 - long linear lesions (AF)
- ▣ Sprinklr
 - Saline cooled tip (VT)



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RF Conductr[®] Catheter

Unique Multi-directional Tip Movement



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Atakr II

100 W RF Generator



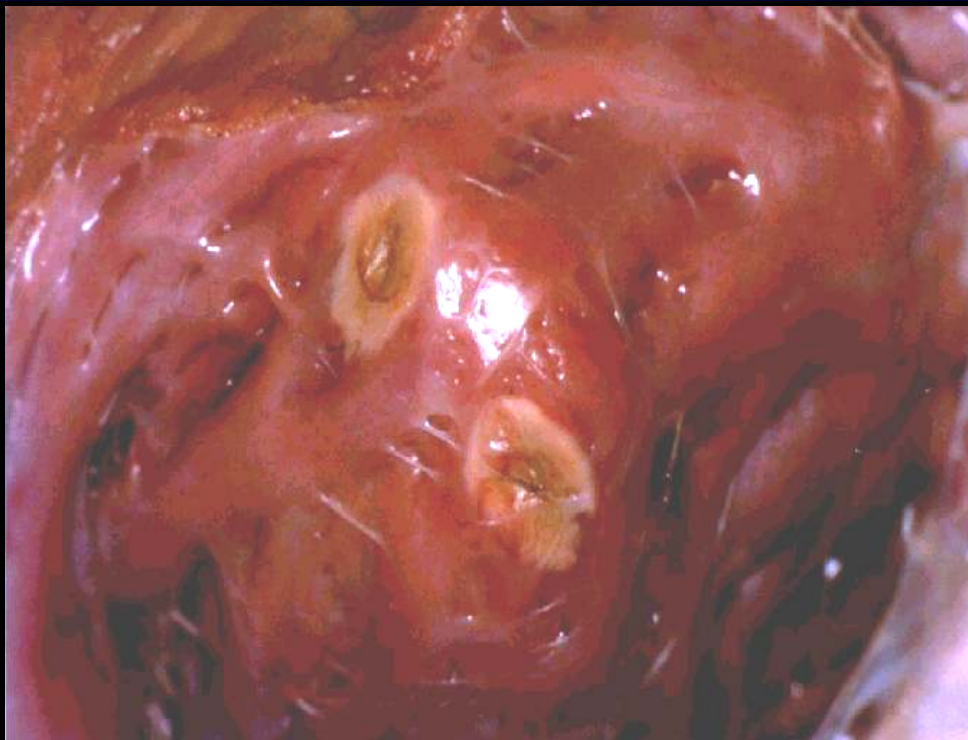
- Low Energy Measurement (pre-ablation RF Therapy quality assessment)
- Up to 100W power
- Data communication with PC or Loca Lisa
- Easy Use
- Many safety features
- Multi programmable
- Prepared for saline cooled catheters
- Temperature or Power controlled ablation therapies



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Results

- ▮ **Small lesions**
- ▮ **Distinct transition zones**



**2 lesions at endocardium
immediately post ablation**



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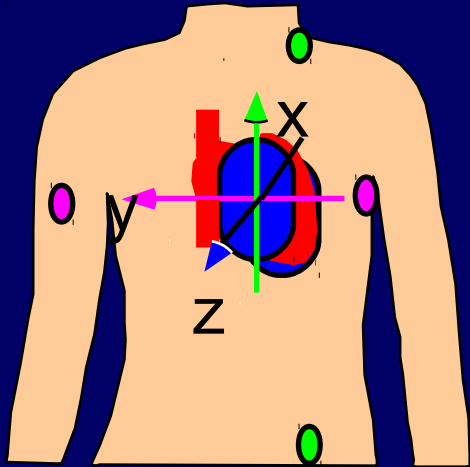
Indications for RF ablation and Success rate

▣ AVNRT	▣ 95%
▣ Atrial Flutter	▣ 90%
▣ AVRT (WPW syndrom)	▣ 95%
▣ Focal arrhythmia (AT or VT)	▣ 85%
▣ Other VT	▣ 60-80%
▣ RVOT	▣ 85%
▣ Atrial Fibrillation	▣ 70-90%

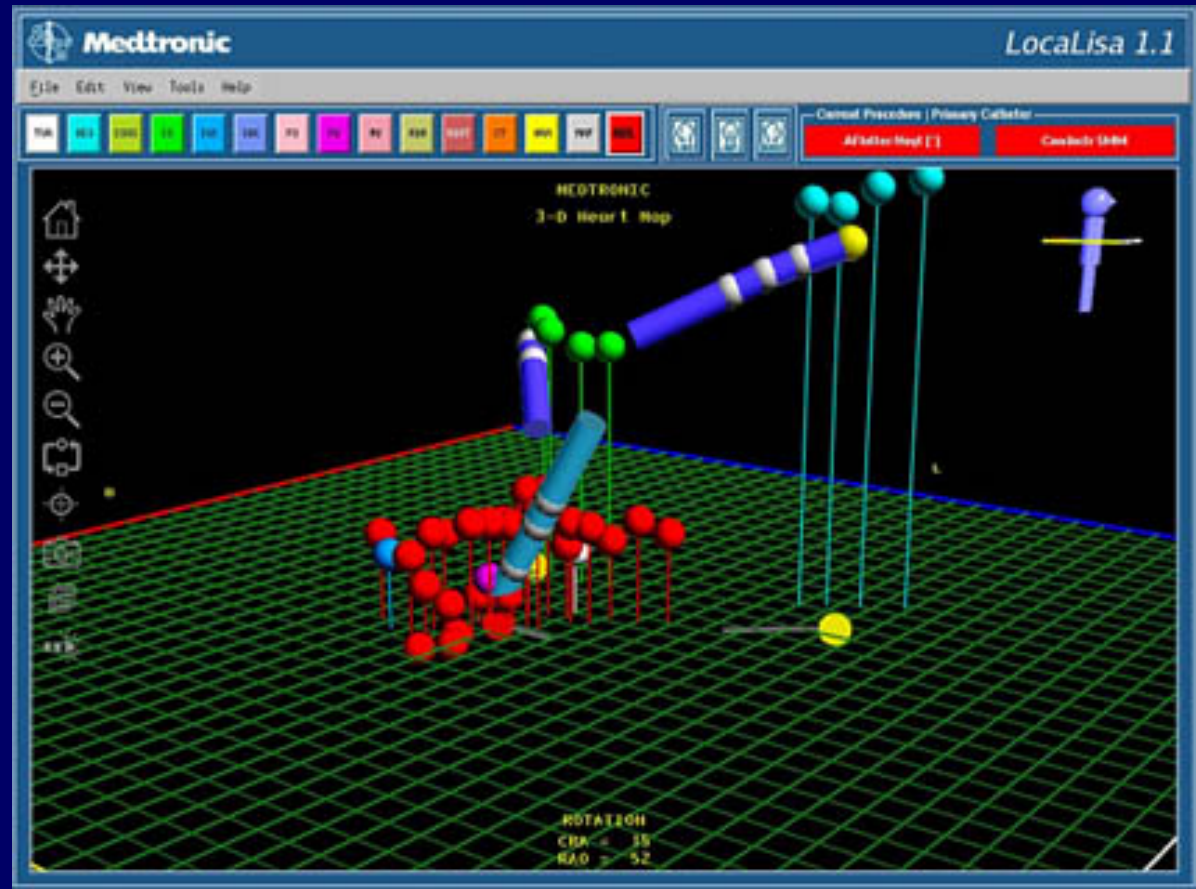


Loca Lisa

a universal navigation tool for EP studies



- 3 pairs of skin electrodes are in an x, y, z orientation around the heart
- Three separate low-power RF fields between electrodes create three orthogonal fields
- Use the voltage at the catheter electrode to determine position of that catheter in 3D space



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Heart Failure Management

Causes of Heart Failure

- **Narrowed arteries**
- **Previous heart attack**
- **High systemic or pulmonary blood pressure**
- **Heart valve disease**
- **Infection or inflammation of heart muscle fibers**



Heart Failure Classifications

NYHA Class

Status

I

No Physical
Limitations

II

Slight Limitations

III

Marked Limitations

IV

Bed-ridden



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Incidence and Prevalence

- ▣ 22 million heart failure patients worldwide
 - (4.7 million in Europe)
- ▣ 700,000 new cases each year
 - (418,000 in Europe)
- ▣ Most common cause of hospital admission over 65 years
- ▣ The only heart disease that is growing in occurrence
- ▣ \$15B est. Annual cost Europe (2% of healthcare)



CRT is a Huge Opportunity

- ▣ **50% reduction in hospitalization rates**
- ▣ **77% fewer hospital days**
- ▣ **JAMA Feb 2003-
51% reduction in Mortality**
- ▣ **CARE HF Study –
First European randomized study to look at CRT on survival, hospitalization and economics**

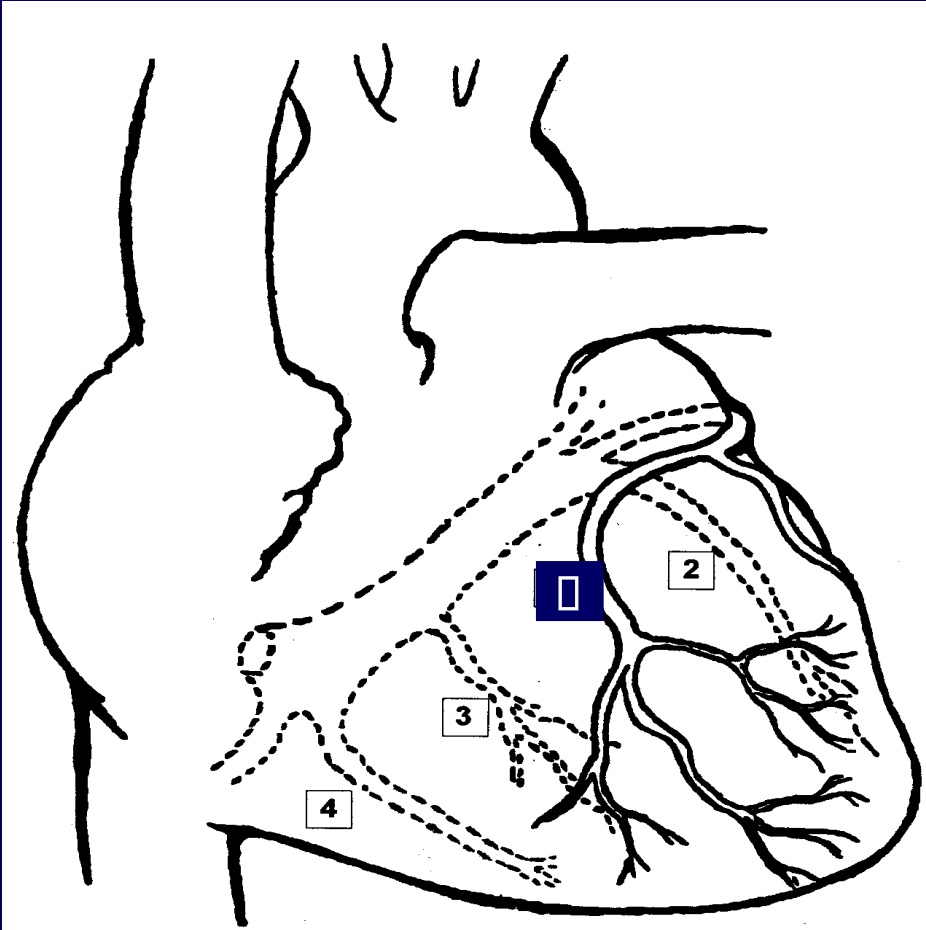


Heart Failure Management



**InSync III Bi-ventricular
Cardiac Stimulator**

Cardiac Venous Anatomy



1. Lateral (marginal) cardiac vein
2. Postero-lateral cardiac vein
3. Posterior cardiac vein
4. Middle cardiac vein
5. Great cardiac vein



Left-heart Leads

ATTAIN OTW

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Med

Pre



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Medtronic CRM...

Common Software/Programmer Architecture

The Programmer
for Half the World's
Devices Today.



Your work is going up the wrong building.
Why should your equipment? To help you simplify product manufacturing,
we provide just one programmer for all of our programmers and 186 - half of
the devices being implanted today. Better design, more efficient
product management. It's obvious we have it all.

9790 *One Efficient Programmer, 186 Devices.*



The Other Half.

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