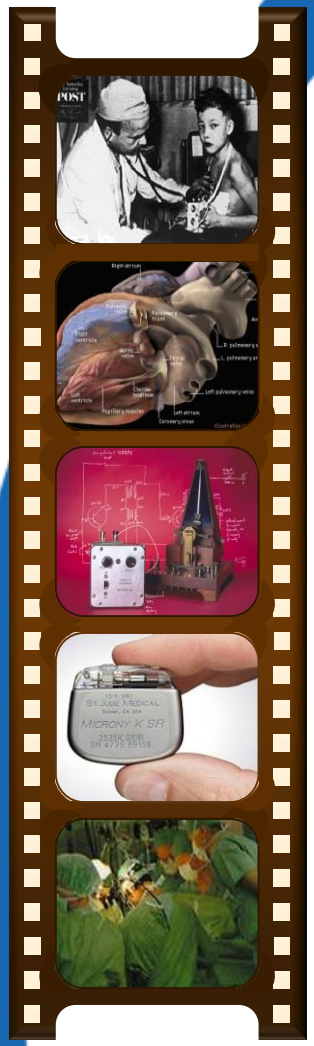


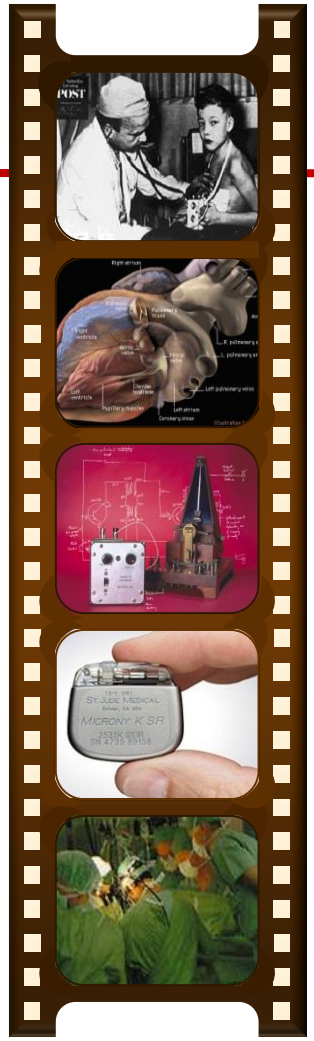
Nouveautés en rythmologie

Dr Sébastien Marchandise

septembre 2016

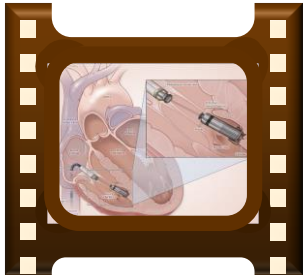
Services de cardiologie
Centre de référence rythmologie - électrophysiologie – stimulation,
Dr C. Barbraud -Pr. Scavée C. – Dr. Marchandise S. – Pr. Le Polain JB.

Cliniques universitaires
SAINT-LUC
UCL BRUXELLES

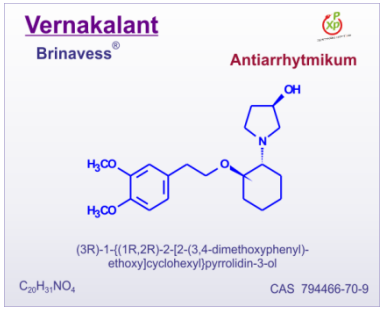


Plan

- **Introduction**
- **Nouveautés pharmacologiques**
  - Vernakalant
  - Edoxaban
  - Antagoniste NOAC
    - Praxbind
    - Andexanet Alfa
- **Nouveautés en stimulation cardiaque**
  - Leadless-pacemaker
  - S-ICD
- **Nouveautés en électrophysiologie invasive**
  - Guidelines 2016 ablation FA



Indications for electrical and pharmacological cardioversion, and choice of antiarrhythmic drugs for pharmacological cardioversion in patients with recent-onset AF.



[a]Ibutilide should not be given when significant left ventricular hypertrophy (≥1.4 cm) is present.
[b]Vernakalant should not be given in moderate or severe heart failure, aortic stenosis, acute coronary syndrome or hypotension. Caution in mild heart failure.
[c]'Pill-in-the-pocket' technique – preliminary assessment in a medically safe environment and then used by the patient in the ambulatory setting.

European Heart Journal (2012) 33, 2719–2747

Vernakalant (BRINAVESS®)

Recommendations for pharmacological cardioversion of recent-onset AF

Recommendations	Class[a]	Level[b]	Ref[c]
When pharmacological cardioversion is preferred and there is no or minimal structural heart disease, intravenous flecainide, propafenone, ibutilide, or vernakalant are recommended.	I	A	120, 121, 123, 124, 126, 127, 131–134
In patients with AF ≤7 days and moderate structural heart disease [but without hypotension <100 mm Hg, NYHA class III or IV heart failure, recent (<30 days) ACS, or severe aortic stenosis], intravenous vernakalant may be considered. Vernakalant should be used with caution in patients with NYHA class I–II heart failure.	IIb	B	120, 121, 124, 128
Intravenous vernakalant may be considered for cardioversion of postoperative AF ≤3 days in patients after cardiac surgery.	IIb	B	122

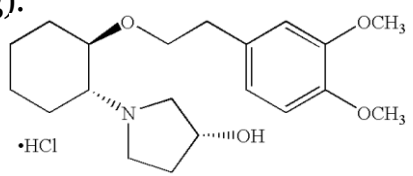
Table 5 Summary of clinical studies of vernakalant in AF/flutter

Study	Design	Number of patients	Underlying heart disease	AF duration	Time to conversion (median), minutes	Conversion to sinus rhythm vs. placebo or control (primary endpoint[a])	Other efficacy outcomes
CRAFT[119]	Double-blind, dose-ranging, placebo-controlled, phase II	56 Vernakalant 2 + 3 mg/kg: *n* = 18; Vernakalant 0.5 + 1 mg/kg: *n* = 18 Placebo: *n* = 20	Hypertension, 57%; diabetes, 23%	AF 3–72 h (mean, 11.5–19.5 h)	14	61% (vernakalant 2 + 3 mg) vs. 5%, *P* <0.001	Conversion rate for vernakalant 0.5 + 1 mg/kg: 11%
ACT I[120]	Double-blind, placebo-controlled, phase III	336 Vernakalant: *n* = 221 Placebo: *n* = 115	Hypertension, 42.5%; ischaemic heart disease, 20.2%; myocardial infarction, 9.8%; heart failure, 14.9%; diabetes, 8%	AF 3 h–45 days (median, 41.8–59.1 h) AF 3 h–7 days (median, 28.2–28.4 h): *n* = 220 AF 8–45 days (median, 19.4–25.5 days): *n* = 116	11	51.7% vs. 4%, *P* <0.001	76% converted after a single dose. Conversion rates for patients with AF ≤48 h: 62.1% vs. 4.9%, *P* <0.001; with AF >7 days: 7.9% vs. 0%, *P* = 0.09
ACT II[122]	Double-blind, placebo-controlled, phase III	160 Vernakalant: *n* = 106 Placebo: *n* = 54	CABG, 67%; valvular surgery, 23.6%; combined, 9.3%. Hypertension, 69.5%; ischaemic heart disease, 80%; heart failure, 31.6%	AF 3–72 h between 24 h and 7 days after cardiac surgery Atrial flutter: *n* = 10	12	47% vs. 14%, *P* <0.001	75% converted after a single dose. Patients with flutter converted: 0/6 vs. 1/4
ACT III[121]	Double-blind, placebo-controlled, phase III	265 Vernakalant: *n* = 134 Placebo: *n* = 131	Hypertension, 43.9%; ischaemic heart disease, 11.8%; myocardial infarction, 6.5%; heart failure, 19.8%; diabetes, 8.4%	AF 3 h–45 days AF 3 h–7 days: *n* = 172 AF 8–45 days: *n* = 70 Atrial flutter: *n* = 23	8	51.2% vs. 3.6%, *P* <0.001	81.8% converted after a single dose. Conversion rates for patients with AF >7 days: 9% vs. 3%, *P* = 0.33; with flutter: 7.1% (1/14) vs. 0% (0/9)
ACT IV[123]	Open-label, phase IV	167	Hypertension, 44%; ischaemic heart disease, 8%; heart failure, 11%	AF 3 h–45 days (median, 38.5 h) AF 3 h–7 days: *n* = 170 AF 8–45 days: *n* = 69	14	50.9%	Conversion rates for patients with AF ≤48 h: 57.9%; with AF >7 days: 11.6%
AVRO[124]	Double-blind, active-controlled (i.v. amiodarone), phase III	232 Vernakalant: *n* = 116 Amiodarone: *n* = 116	Hypertension, 71.6%; ischaemic heart disease, 22.4%; myocardial infarction, 8.2%; heart failure, 19.8%, (NYHA I, 45.7%, NYHA II, 54.3%); valvular heart disease, 6.9%	AF 3–48 h (median, 17.7 h)	11	51.7% vs. 5.2%, *P* <0.0001	Reduction in symptoms at 2 h reported by 53.4% patients in the vernakalant group vs. 32.8% in the amiodarone group, *P* = 0.0012
Scene 2[129]	Double-blind, controlled, phase II/III	54 Vernakalant: *n* = 39 Placebo: *n* = 15	–	Atrial flutter 3 h–45 days (mean, 98–178 h)	–	3% vs. 0%, *P* = 0.45	–

European Heart Journal (2012) 33, 2719–2747

Vernakalant (BRINAVESS®)

- **Posologie** : 3 mg/kg IV sur 10 min. A répéter dans les 15 minutes si nécessaire (2 mg/kg).



Vernakalant Hydrochloride

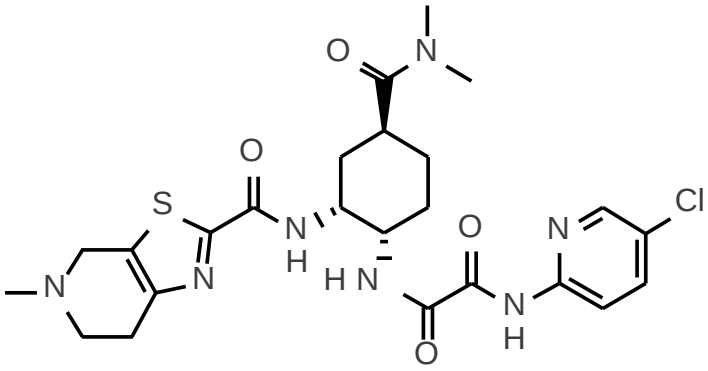
- **Contre-indications:**
  - Hypersensibilité au médicament
  - Sténose aortique sévère, TA< 100 mmHg, insuffisance cardiaque NYHA III et NYHA IV.
  - QT long, bradycardie sévère, dysfonction sinusale BAV 2 et BAV 3 sans pacemaker.
  - Administration d'AAR (classe I et classe III) IV dans les 4 heures précédant l'administration.
  - Syndrome coronarien aigu au cours des 30 jours précédents

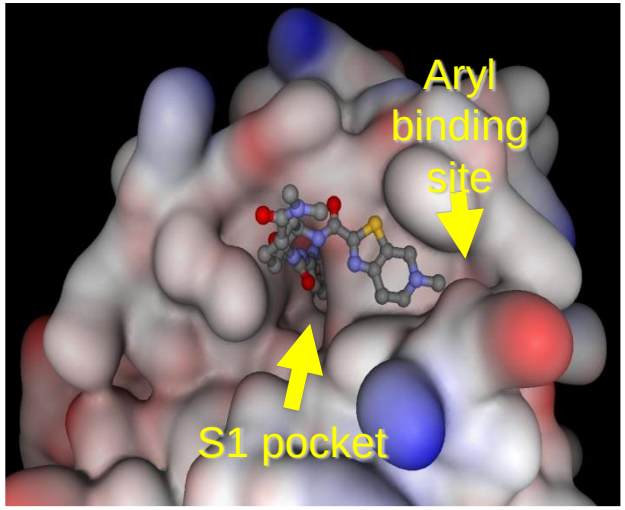
- **Effets secondaires**
  - altération du goût (30%), des éternuements (16%), paresthésie (10%) et des nausées (9%), (résolutifs en 5-15 minutes).
  - Une hypotension transitoire (5-7%)
  - Une bradycardie
  - Arythmies ventriculaires non soutenues (triplets ventriculaires et des salves)
  - Prolongement intervalle QTc de 20-25 ms, élargissement QRS (8 ms)

Administré par du personnel médical qualifié, dans des conditions de surveillance clinique appropriées pour la cardioversion.

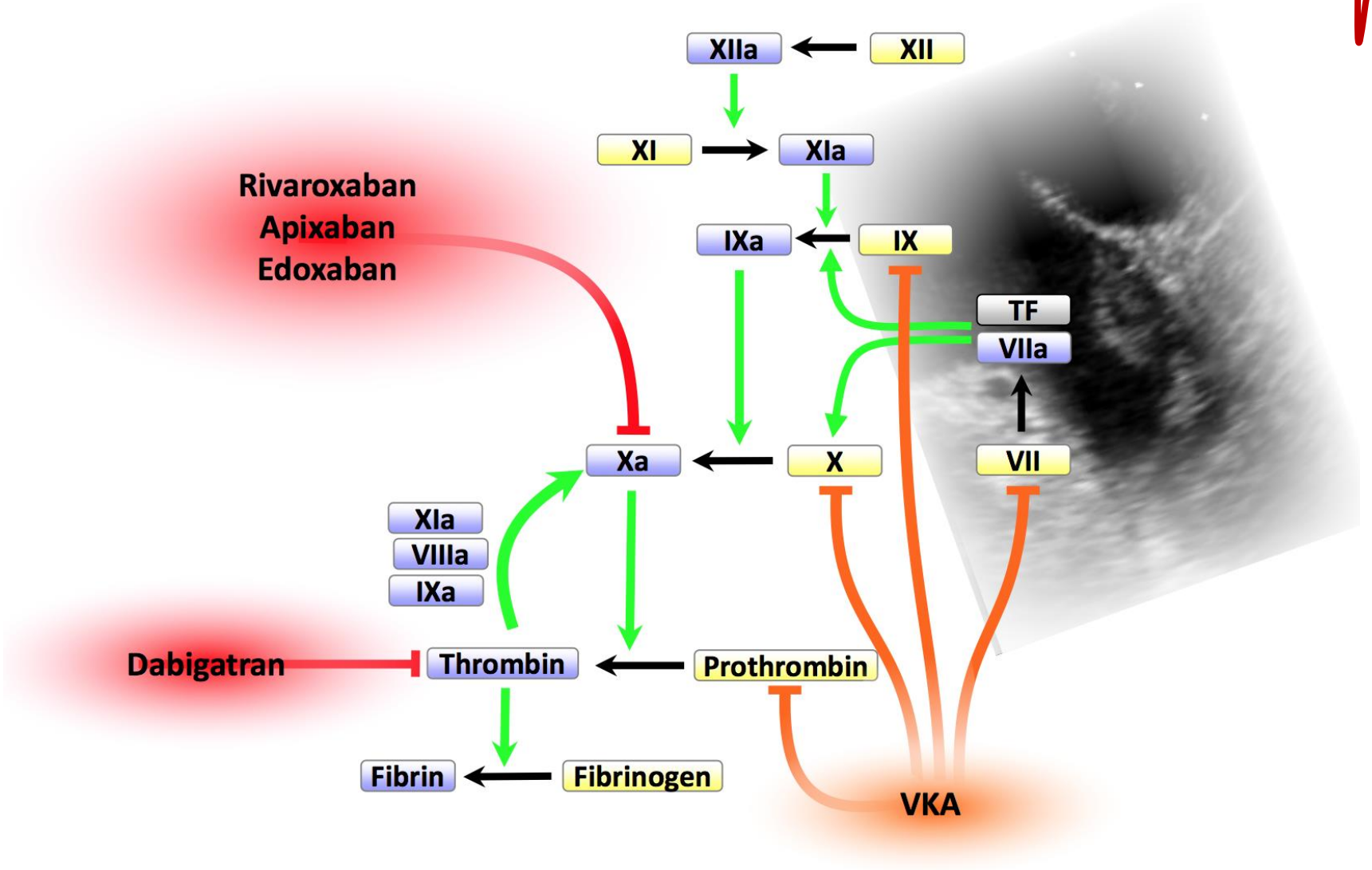
Pharmacokinetics and pharmacodynamics of Lixiana, Edoxaban®

- Reversible oral direct factor Xa inhibitor
- ~62% oral bioavailability
- Rapid onset of action (within 1–2hrs)
- ~50% of the absorbed dose is cleared renally
- Plasma elimination half-life: 10 to 14 hours
- No or minimal impact of food
- Substrate of the P-glycoprotein drug transporter
- CYP metabolism is less than 10%





– VKA and NOACS -



Mod. nach Steffel & Braunwald, European Heart Journal 2011

– Guidelines -

In patients with a CHA_2DS_2-VASc score of 0 (i.e., aged <65 years with lone AF) who are at low risk, with none of the risk factors, no antithrombotic therapy is recommended.	I	B
Where OAC is recommended, one of the NOACs, either: • a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] … should be considered rather than adjusted-dose VKA (INR 2–3) for most patients with non-valvular AF, based on their net clinical benefit.	IIa	A
• a direct thrombin inhibitor (dabigatran); or • an oral factor Xa inhibitor (e.g., rivaroxaban, apixaban)[d] …. should be considered, based upon an assessment of the risk of bleeding complications and patient preferences.	IIa	A

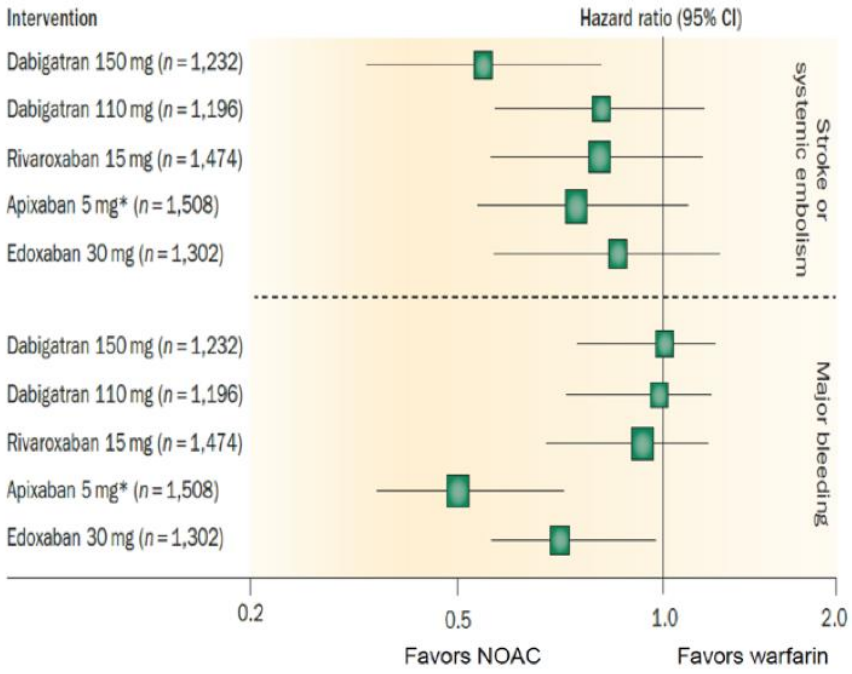
Quel NOAC utiliser….?

Si altération de la fonction rénale

Table 3: Major efficacy (analysed as intention to treat) and safety outcomes in the atrial fibrillation studies (10–12). Hazard ratios or relative risks are in relation to warfarin and are in bold type when showing a statistically significant reduction.

Efficacy (reduction of stroke or systemic embolism)	Safety (major bleeding)
Best	
Dabigatran 150 mg BID **RR 0.66 (95% CI, 0.53–0.82)**	Edoxaban 30 mg daily **HR 0.47 (97.5% CI, 0.41–0.55)**
Apixaban 5 mg BID **HR 0.79 (95% CI, 0.66–0.95)**	Apixaban 5 mg BID **HR 0.69 (95% CI, 0.60–0.80)**
Edoxaban 60 mg daily HR 0.87 (97.5% CI, 0.73–1.04)	Dabigatran 110 mg BID **RR 0.80 (95% CI, 0.69–0.93)**
Rivaroxaban 20 mg daily HR 0.88 (95% CI, 0.74–1.03)	Edoxaban 60 mg daily **HR 0.80 (97.5% CI, 0.71–0.91)**
Dabigatran 110 mg BID RR 0.91 (95% CI, 0.74–1.11)	Dabigatran 150 mg BID RR 0.93 (95% CI, 0.81–1.07)
Edoxaban 30 mg daily HR 1.13 (97.5% CI, 0.96–1.34)	Rivaroxaban 20 mg daily HR 1.04 (95% CI, 0.90–1.20)
Worst*	

RR, relative risk; HR, hazard ratio; CI, confidence interval; BID, twice daily.
*Note that "worst" risk estimate is still non-inferior to warfarin.



Schulman S. Thrombosis and Haemostasis 2014;111(4):575-582

Deepak L. Bhatt Circulation. 2016;133:1512-1515

Major bleedings occur with all NOACs

	Dabigatran RE-LY (Connolly, 2009 en 2010)	Dabigatran Following registered indication (Lip 2014)	Apixaban ARISTOTLE (Granger 2011)	Rivaroxaban ROCKET-AF (Patel, 2011)
Intracranial bleeding (%/year)	Warfarine: 0.74 Dabigatran150 mg: 0.30 Dabigatran 110 mg: 0.23	Warfarine: 0.77 Dabigatran: 0.22	Warfarine : 0.80 Apixaban : 0.33	Warfarine: 0.70 Rivaroxaban: 0.50
Major bleeding (%/year)	Warfarine: 3.36 Dabigatran150 mg: 3.11 Dabigatran 110 mg: 2.71	Warfarine: 3.55 Dabigatran: 3.02	Warfarine :3.09 Apixaban : 2.13	Warfarine: 3.40 Rivaroxaban: 3.60
Life-threatening bleeding (%/year)	Warfarine: 1.80 Dabigatran150 mg: 1.45 Dabigatran 110 mg: 1.22	Warfarine: 1.75 Dabigatran: 1.28	Warfarine :1.13 Apixaban : 0.52 (severe bleeding)	Warfarine: 1.20 Rivaroxaban: 0.80 (critical bleeding)

Currently available aspecific treatments to revert OAC-induced coagulopathy

3- and 4-Factor PCC, FFP, rFVIIa

- Repletion of coagulation factors in the blood
- Used for managing severe bleeding in VKA- and NOAC-treated patients*
- Not registered to prevent bleeding in emergency surgery/urgent procedure
- PCC, rFVIIa: prothrombotic risk
  FFP: risk of fluid overload

Vitamin K

- Only for VKA-treated patients, not NOACs
- Restores physiological clotting factor synthesis via a slow and complex process with clinically significant variability between patients[1]
- INR corrects more quickly than coagulopathy

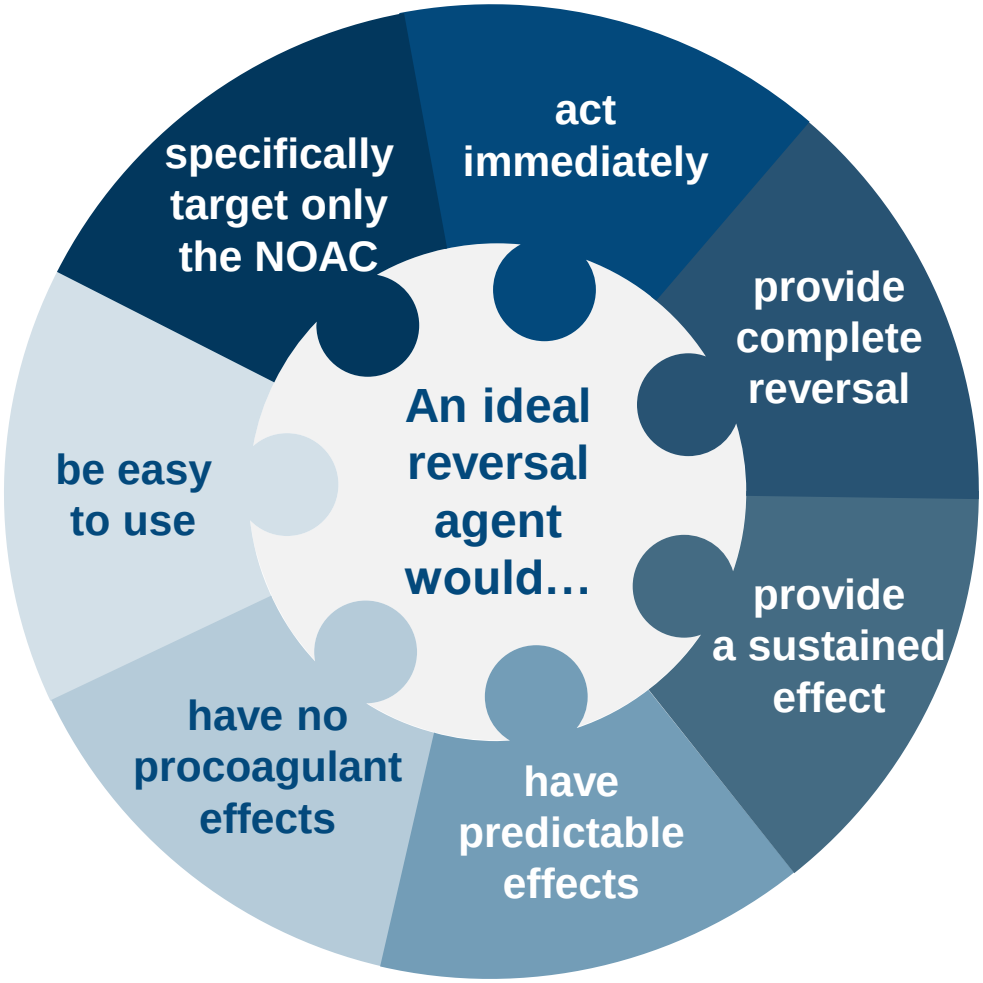
[see Supplementary Material for further information]

A specific reversal agent will be the preferred option to restore coagulation in NOAC-treated patients when rapid reversal is required

*Not approved for NOAC-treated patients, but listed in EU NOAC labels and in guidelines/expert statements as treatment option in cases of severe haemorrhage with NOAC; FFP, fresh frozen plasma; INR, international normalized ratio; PCC, prothrombin complex concentrate; rFVIIa, recombinant Factor VIIa; VKA, Vitamin K antagonist

1. Hanley et al. J Clin Pathol 2004;57:1132–39

What are the desirable characteristics of a reversal agent?



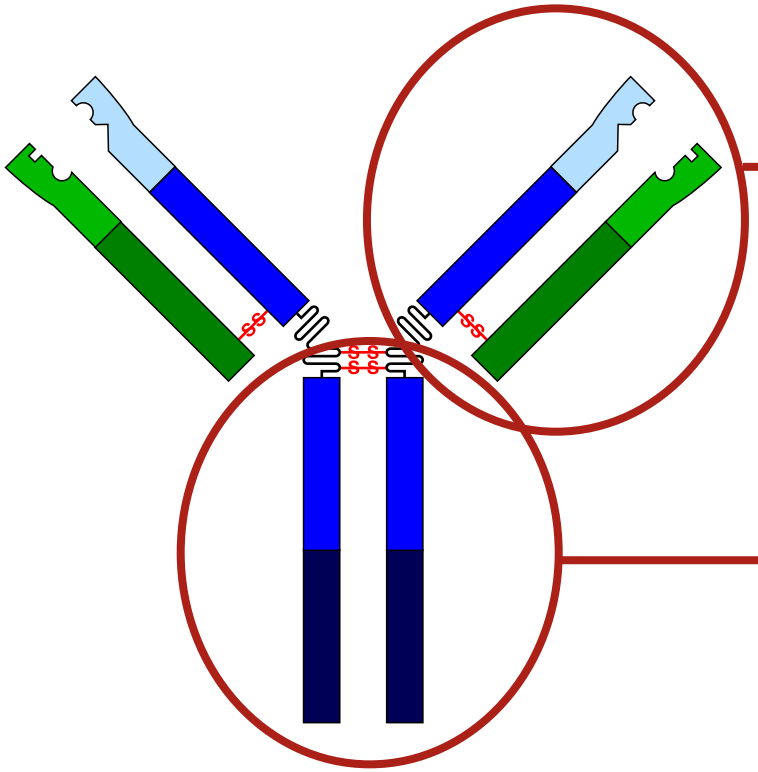
Emergency surgery or urgent intervention

Life-threatening or uncontrolled bleeding

Idarucizumab is a humanized monoclonal antibody fragment developed and produced by BI

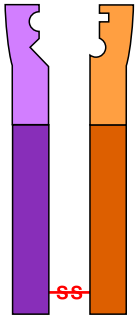
A monoclonal mouse antibody was developed with high dabigatran binding affinity

Idarucizumab is the humanized Fab fragment expressed directly in hamster cells and produced in-house by BI



Fab region

- This is the part of the antibody that binds to dabigatran

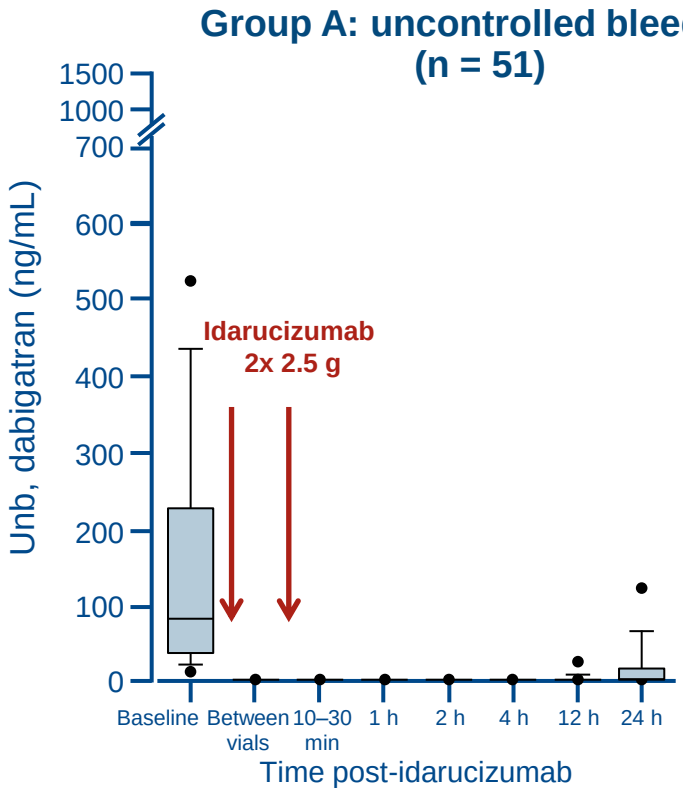


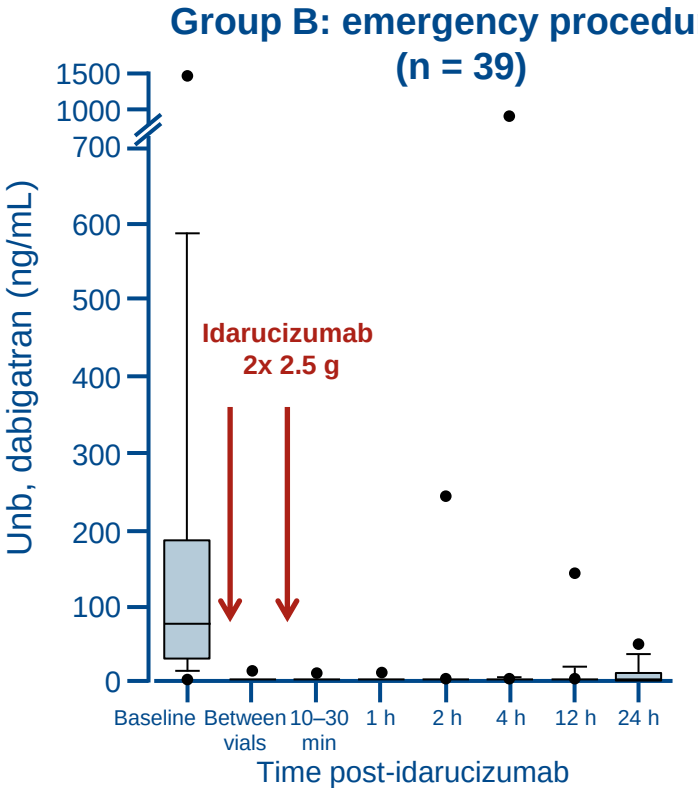
Fc region removed

- This is a structural element and interacts with the immune system
- Non-specific binding is avoided by removal of the Fc region

van Ryn J. AHA 2012; presentation 9928

Dabigatran levels were reduced immediately after idarucizumab administration



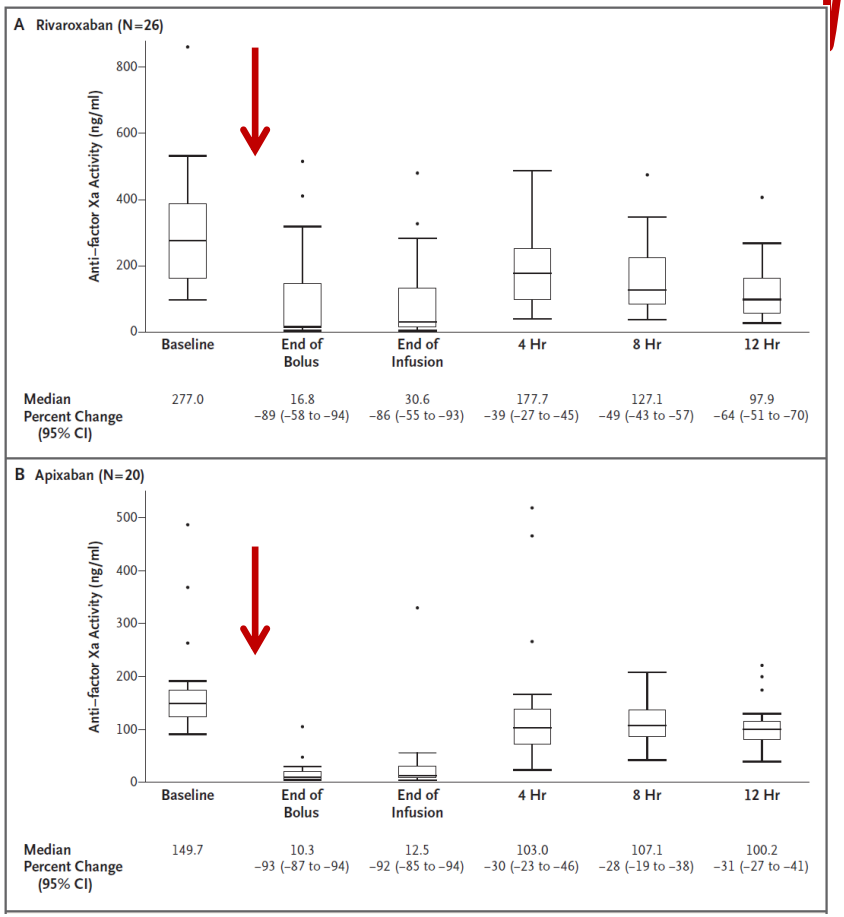


Dabigatran levels were <20 ng/mL* in 89/90 patients after infusion of first vial, in 77/83 at 12 hours and 62/78 patients at 24 hours

*A level that produces little or no anticoagulant effect. Pollack et al. N Engl J Med 2015

Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors

- Multicenter, prospective, open-label, single-group study.
- 67 patients
- Acute major bleeding within 18 hours after the administration of a factor Xa inhibitor
- bolus of andexanet followed by a 2-hour infusion of the drug
- Gastrointestinal or intracranial bleeding.

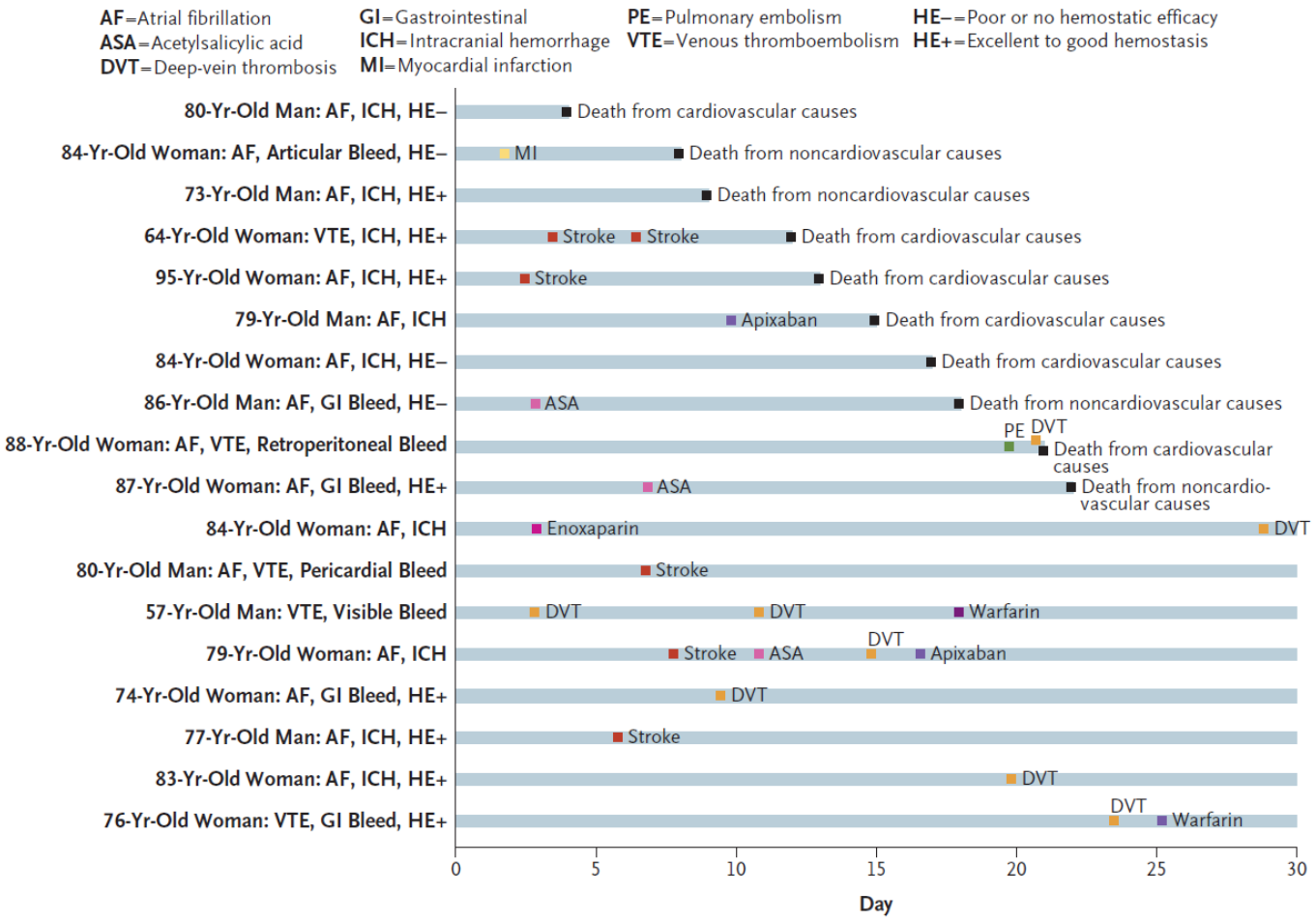


After the bolus administration, the median anti– factor Xa activity decreased by 89% (95% confidence interval [CI], 58 to 94) from baseline among patients receiving rivaroxaban and by 93% (95% CI, 87 to 94) among patients receiving apixaban.

Annexa-4 study NEJM 2016 august, 30

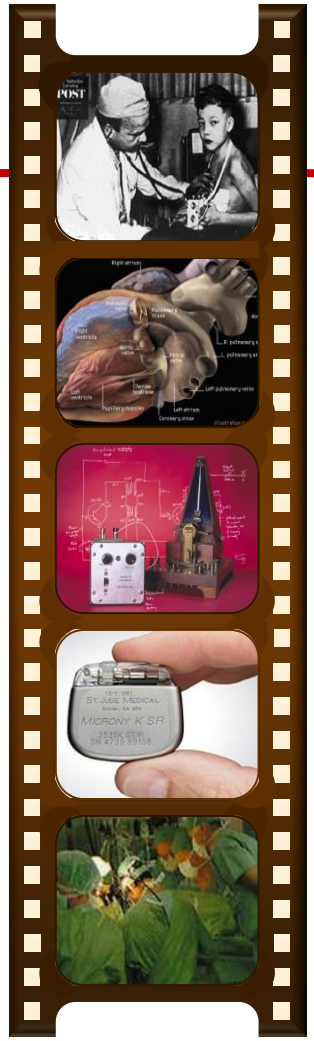
Andexanet Alfa for Acute Major Bleeding Associated with Factor Xa Inhibitors

Thrombotic Events or Death during the 30-Day Study Period.



Thrombotic events occurred in 12 of 67 patients (18%) during the 30-day follow-up

Annexa-4 study NEJM 2016



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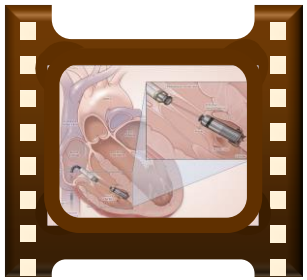
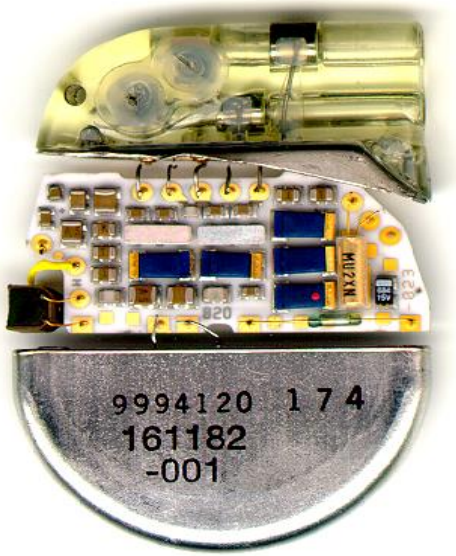
  - Guidelines 2016 ablation FA



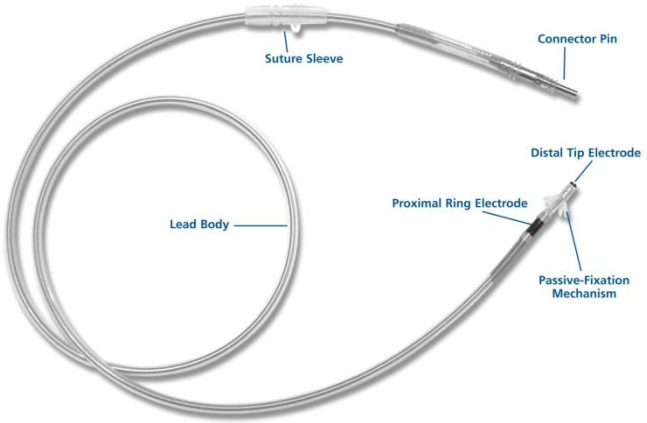
Human Pacemaker history…



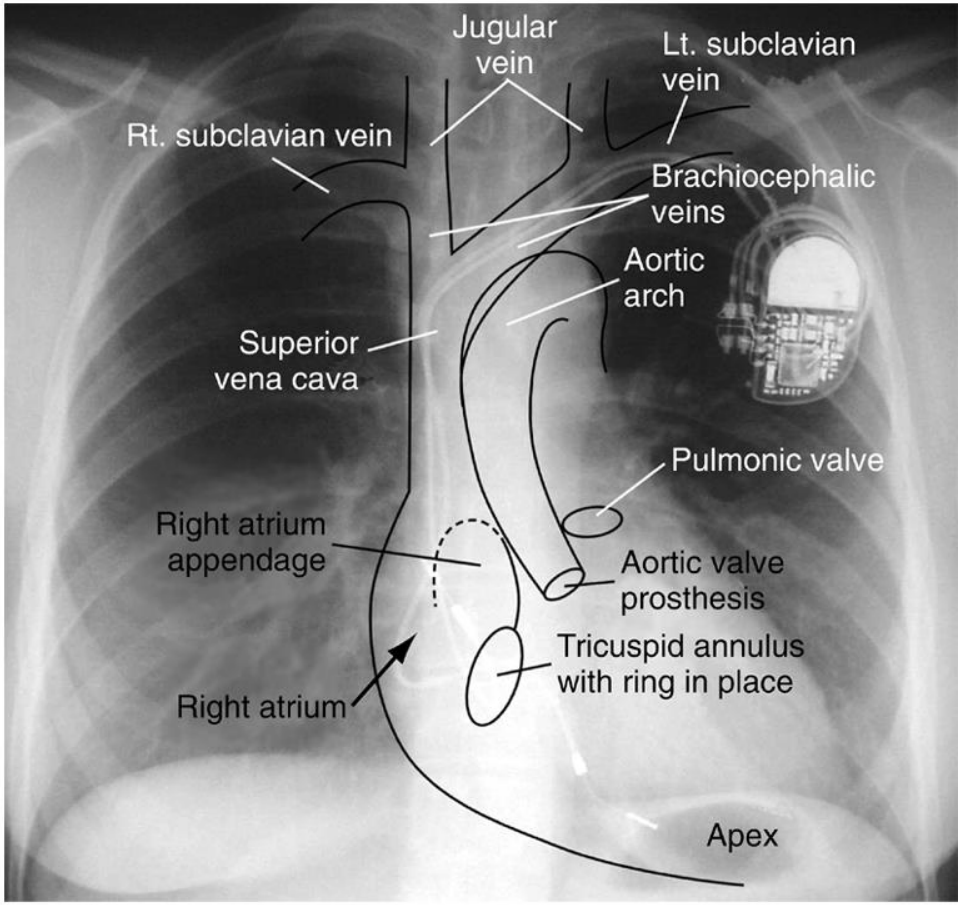
Connector

Electronic Circuits

Battery



Lead



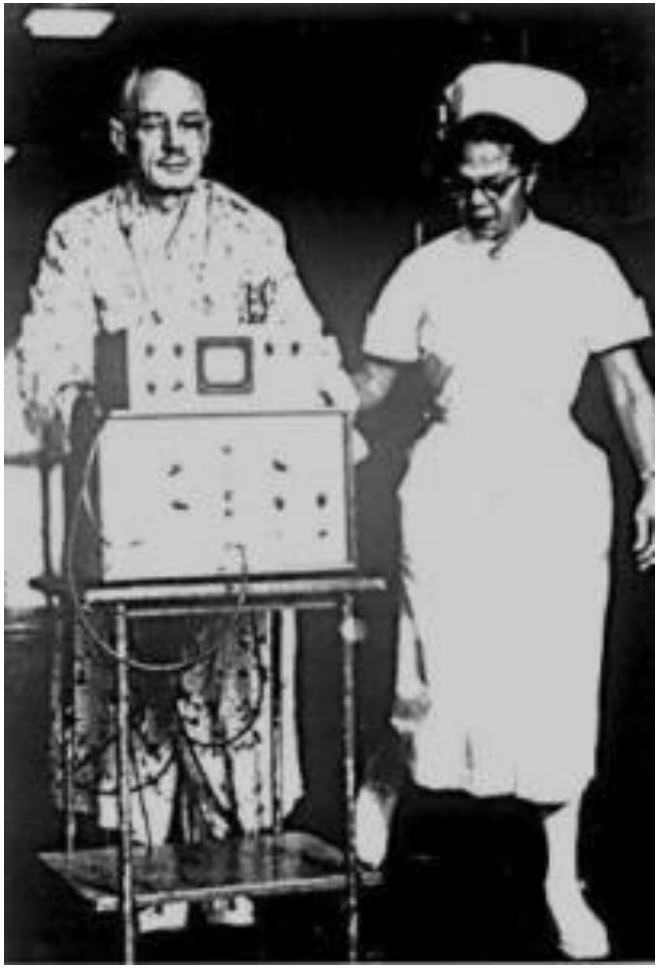
> 650 000 PCMK/years

Castle LW, Cook S: Pacemaker radiography. In Ellenbogen KA, Kay GN, Wilkoff BL [eds]: Clinical Cardiac Pacing. Philadelphia, WB Saunders, 1995, p 538.

First human external pacemaker

⇨ *1952*

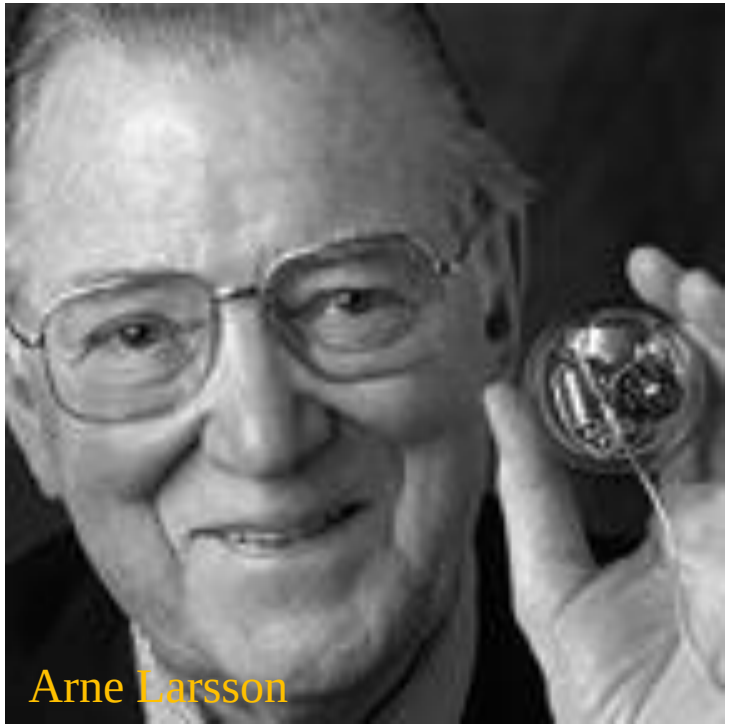
Paul Zoll (1911-1999)



PM-65 by Paul Zoll allowed the patient to ambulate (1955)

First human with fully implanted pacemaker

⇨ *1958*



Born May 26, 1915 and died December 28, 2001 in Stockholm, at age 86 years. Arne Larsson benefit from 26 different pacemakers over 43 years of his life

Human Pacemaker history…

First implanted
Elmqvist's pacemaker
Weight: 73,4 gr
Size: 35 cc

1958

First implantable
Pacemaker
Chardck – Greatbach

1960

Activitrax
Medtronic
First rate response

1984

Thera™
First
mode switching

1995

Full automaticity
MRI safe
Weight: 20 gr
Size: 12 cc

2010

Leadless
Pacemaker
Weight: 2 gr
Size: 0,8 cc

2013

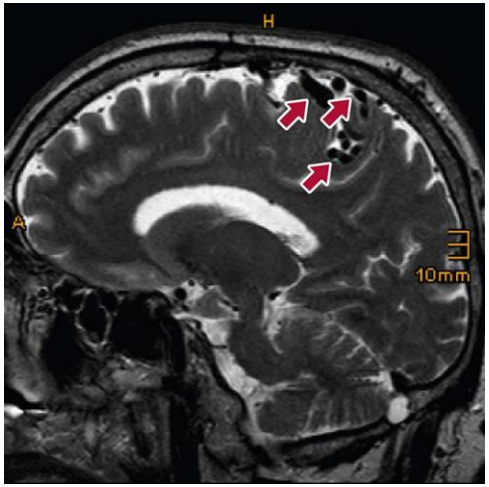
- Heavy surgery
- Abdominal can, epicardial leads
- Non programmable
- Indication: BAV III, surgery
- Longevity : Weeks

- Local anesthesia
- Venous acces
- Fully programmable
- Full automaticity
- AAI safe R algorythm
- Guidelines
- MRI safe
- Longevity : > 7 Y

MRI and pacemaker

Yet 50-75% of cardiac device patients will be indicated for a MRI scan over the lifetime of their device*

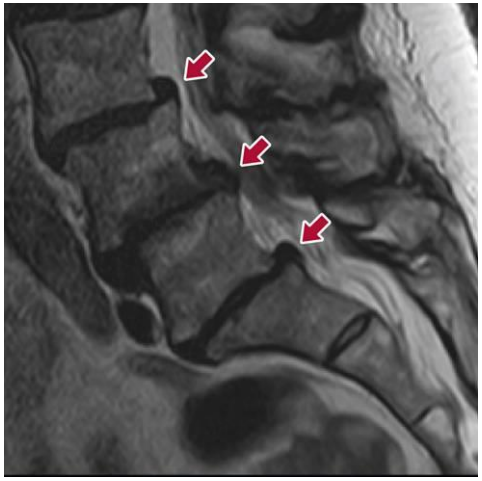
- MRI is gold standard for soft tissue imaging



Head (Brain)

38y-old man with a history of long-standing focal seizures

Arteriovascular malformation in the brain parenchyma with dilated vessels



Lumbar spine

75y-old woman with lower back and bilateral leg pain

Multiple disc herniations in the lumbar spine at segments L3-4, L4-5 and L5-S1

* Kalin R, Stanton MS, Current clinical issues for MRI scanning of pacemaker and defibrillator patients, Pacing Clin Electrophysiol, Apr 2005, 28(4): 326–8.

MR conditional by design

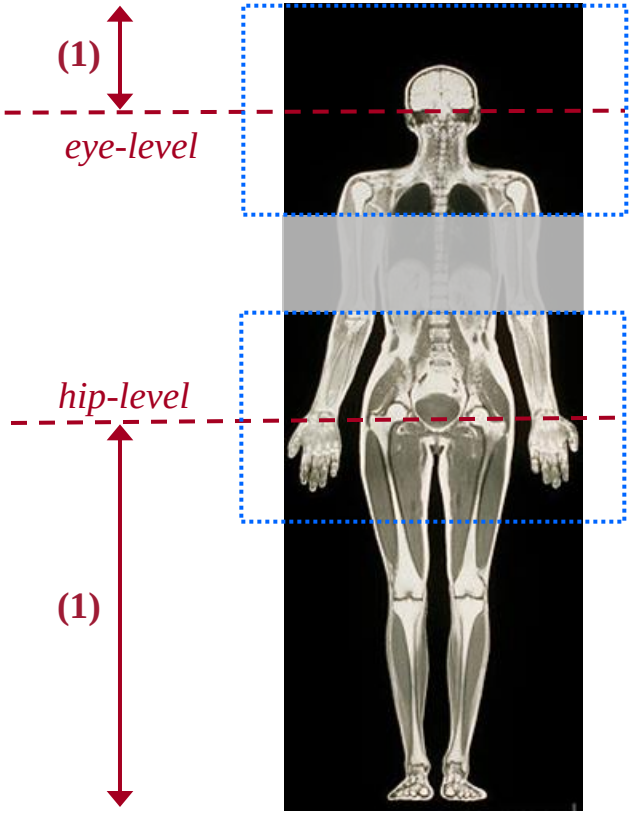
- Strict reduction of ferromagnetic components
- Special protection circuits in the ICD hardware
- Dedicated device program settings during MR examination
- MR-optimized component arrangements and material combinations

Excursion: ProMRI® scanning capabilities

ProMRI® scan conditions

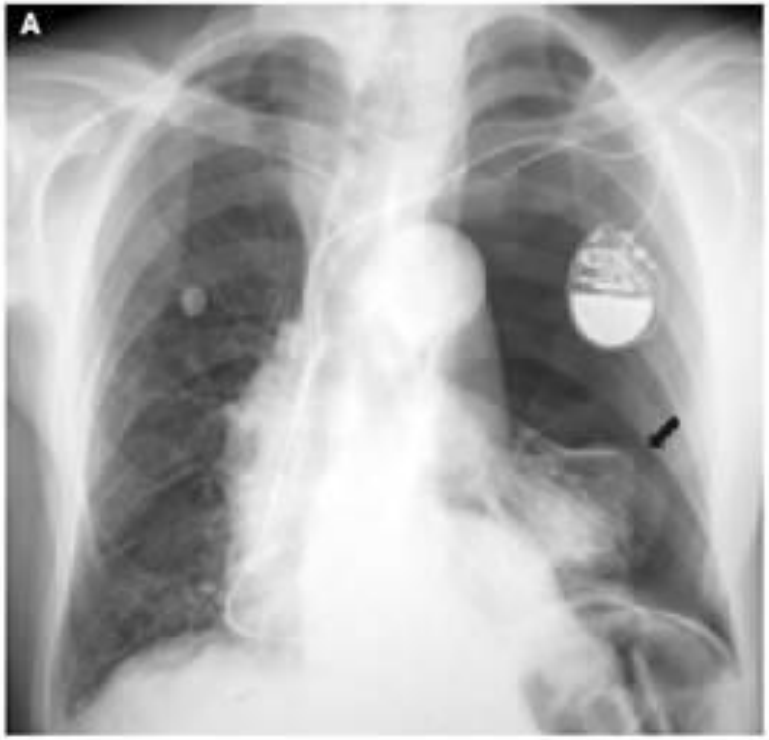
- **Pacemaker implanted > 2 months**
- **Control regularly**
- **Check before and after MRI**
- **Pacemaker AND leads proMRI**

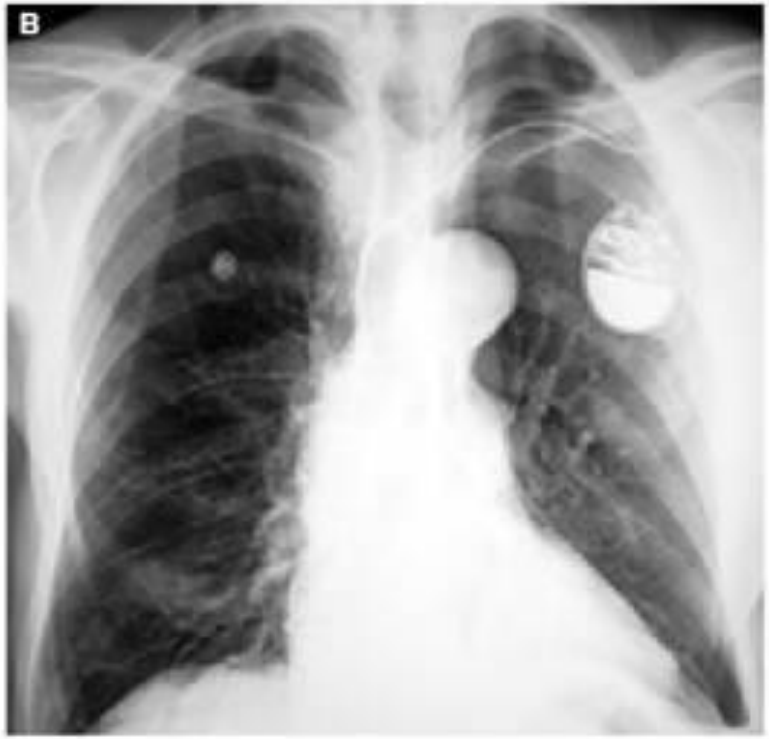
- ***1.5 → 3 Tesla MR***
- ***SAR ≤ 2.0 W/kg (Head ≤ 3,2 W/kg)***
- ***Permissible isocenter positioning zone (1)***

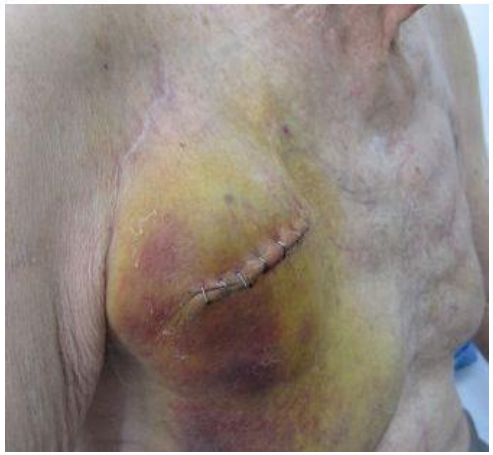


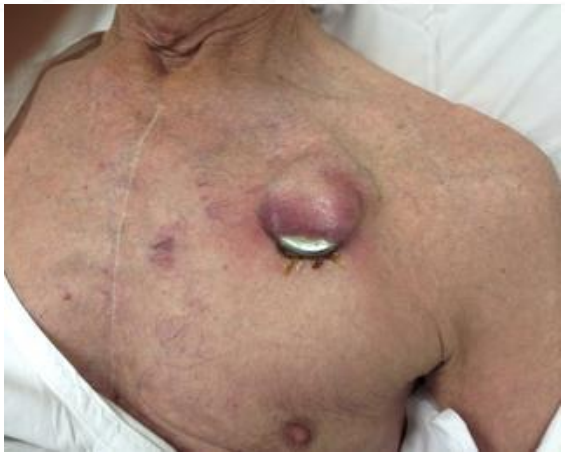
Assumed patient size 175cm

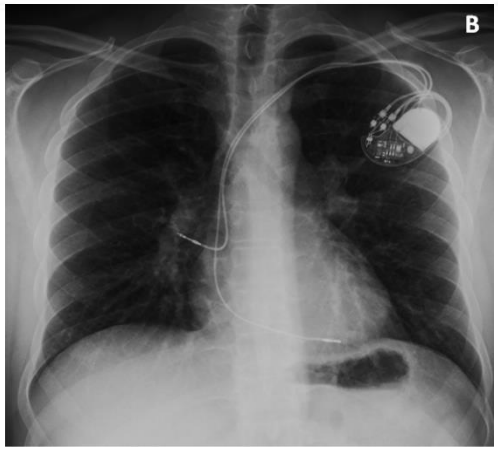
Complications after cardiac implantable electronic device implantations











Complications after cardiac implantable electronic device implantations

	All (n = 5918)	New implant (n = 4355)	Generator replacement (n = 1136)	Upgrade/ lead revision (n = 427)
Any complication	562 (9.5; 8.7–10.2)	432 (9.9; 9.0–10.8)	67 (5.9; 4.5–7.3)	63 (14.8; 11.4–18.1)
Any major complication	329 (5.6; 5.0–6.1)	253 (5.8; 5.1–6.5)	40 (3.5; 2.4–4.6)	36 (8.4; 5.8–11.1)
Any minor complication	250 (4.2; 3.7–4.7)	189 (4.3; 3.7–4.9)	30 (2.6; 1.7–3.6)	31 (7.3; 4.8–9.7)
Major complications				
Lead related re-intervention	143 (2.4; 2.0–2.8)	120 (2.8; 2.3–3.2)	10 (0.9; 0.3–1.4)	13 (3.0; 1.4–4.7)
Infection	49 (0.8; 0.6–1.1)	24 (0.6; 0.3–0.8)	17 (1.5; 0.8–2.2)	8 (1.9; 0.6–3.2)
Local infection	22 (0.4; 0.2–0.5)	10 (0.2; 0.1–0.4)	8 (0.7; 0.2–1.1)	4 (1.0; 0.0–1.9)
Systemic infection/endocarditis	27 (0.5; 0.3–0.6)	14 (0.3; 0.2–0.5)	9 (0.8; 0.3–1.3)	4 (0.9; 0.0–1.9)
Pneumothorax requiring drainage	51 (0.9; 0.6–1.1)	45 (1.0; 0.7–1.3)	0	6 (1.4; 0.3–2.5)
Cardiac perforation	38 (0.6; 0.4–0.8)	35 (0.8; 0.5–1.1)	0	3 (0.7; 0.0–1.5)
No intervention	21 (0.4; 0.2–0.5)	18 (0.4; 0.2–0.6)	0	3 (0.7; 0.0–1.5)
Intervention[b]	17 (0.3; 0.2–0.4)	17 (0.4; 0.2–0.6)	0	0
Pocket revision because of pain	25 (0.4; 0.3–0.6)	10 (0.2; 0.1–0.4)	9 (0.8; 0.3–1.3)	6 (1.4; 0.3–2.5)
Generator-lead interface problem with re-intervention	7 (0.1; 0.0–0.2)	3 (0.1; 0.0–0.1)	4 (0.4; 0.0–0.7)	0
Haematoma requiring re-intervention	10 (0.2; 0.1–0.3)	9 (0.2; 0.1–0.3)	1 (0.1; 0.0–0.3)	0
Other[c]	16 (0.3; 0.1–0.4)	16 (0.4; 0.2–0.5)	0	0
Minor complications				
Haematoma[d]	138 (2.3; 1.9–2.7)	104 (2.4; 1.9–2.8)	20 (1.8; 1.0–2.5)	14 (3.3; 1.6–5.0)
Wound infection treated with antibiotics	69 (1.2; 0.9–1.4)	47 (1.1; 0.8–1.4)	12 (1.0; 0.5–1.7)	10 (2.3; 0.9–3.8)
Pneumothorax conservatively treated	39 (0.7; 0.5–0.9)	32 (0.7; 0.5–1.0)	0	7 (1.6; 0.4–2.8)
Lead dislodgement without re-intervention	10 (0.2; 0.1–0.3)	9 (0.2; 0.1–0.3)	0	1 (0.2; 0.0–0.7)

European Heart Journal (2014) 35, 1186–1194

Human Pacemaker history…

First implanted
Elmqvist's pacemaker
Weight: 73,4 gr
Size: 35 cc

1958

First implantable
Pacemaker
Chardck – Greatbach

1960

Activitrax
Medtronic
First rate response

1984

Thera™
First
mode switching

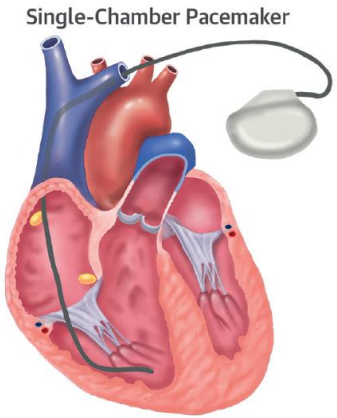
1995

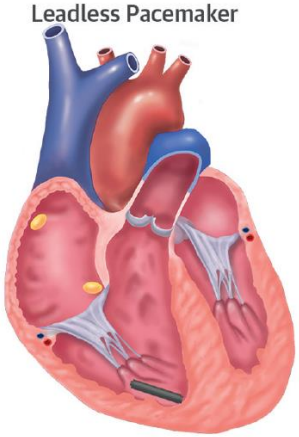
Full automaticity
MRI safe
Weight: 20 gr
Size: 12 cc

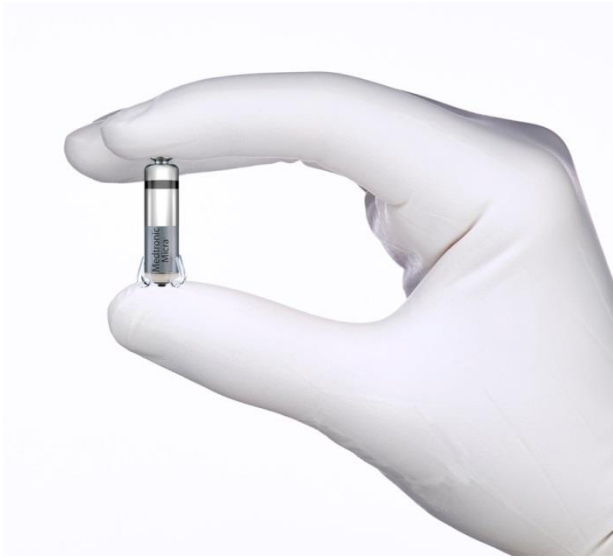
2010

Leadless
Pacemaker
Weight: 2 gr
Size: 0,8 cc

2013



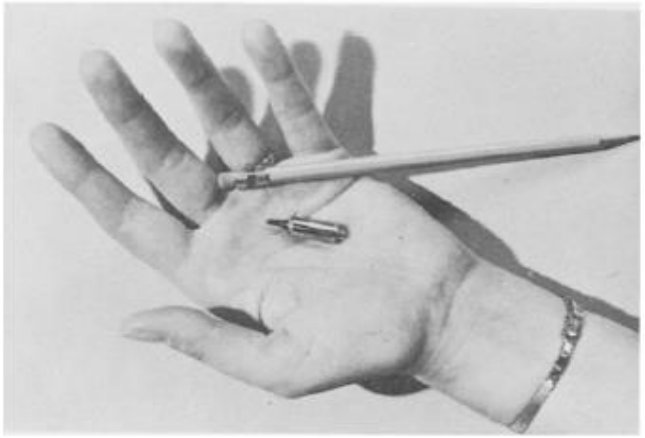




JACC, 2015; 65: 1505–8

Totally Self-Contained Intracardiac Pacemaker*

J. WILLIAM SPICKLER, PH.D., NED S. RASOR, PH.D.†, PAUL KEZDI, M.D.
S. N. MISRA, M.D., K. E. ROBINS, P.E., AND CHARLES LeBOEUF, P.E.



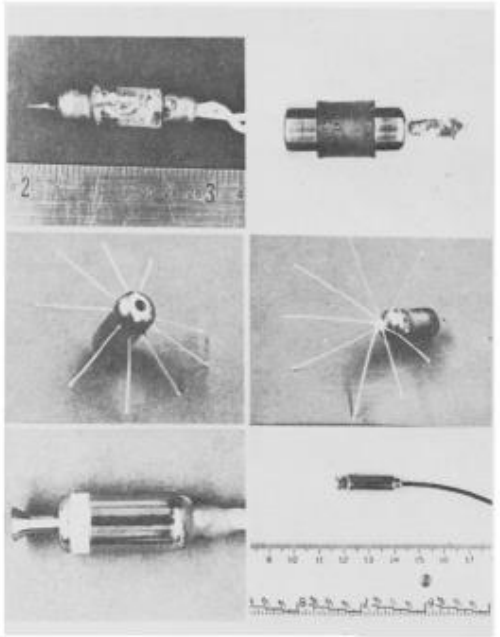
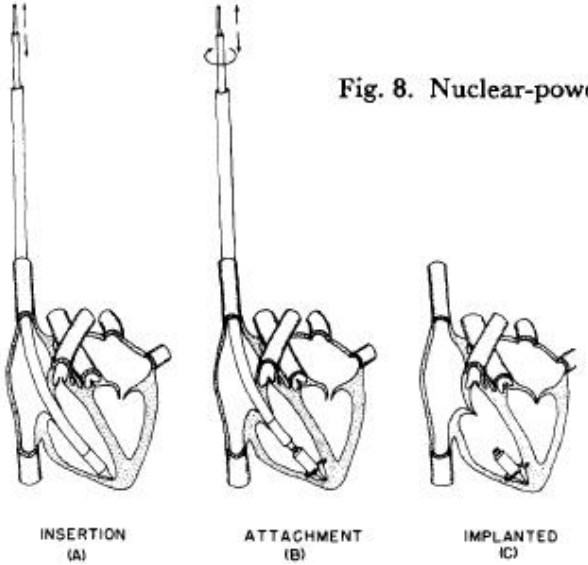
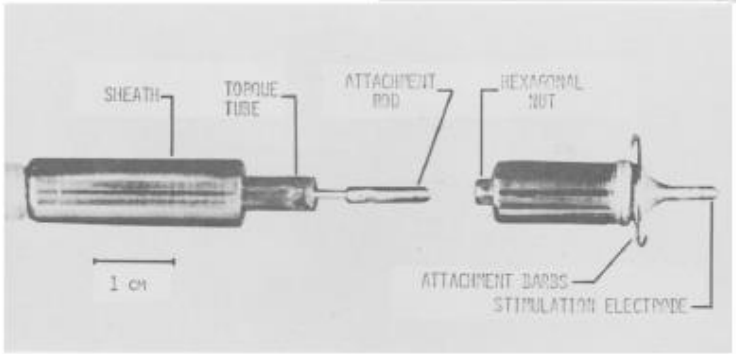
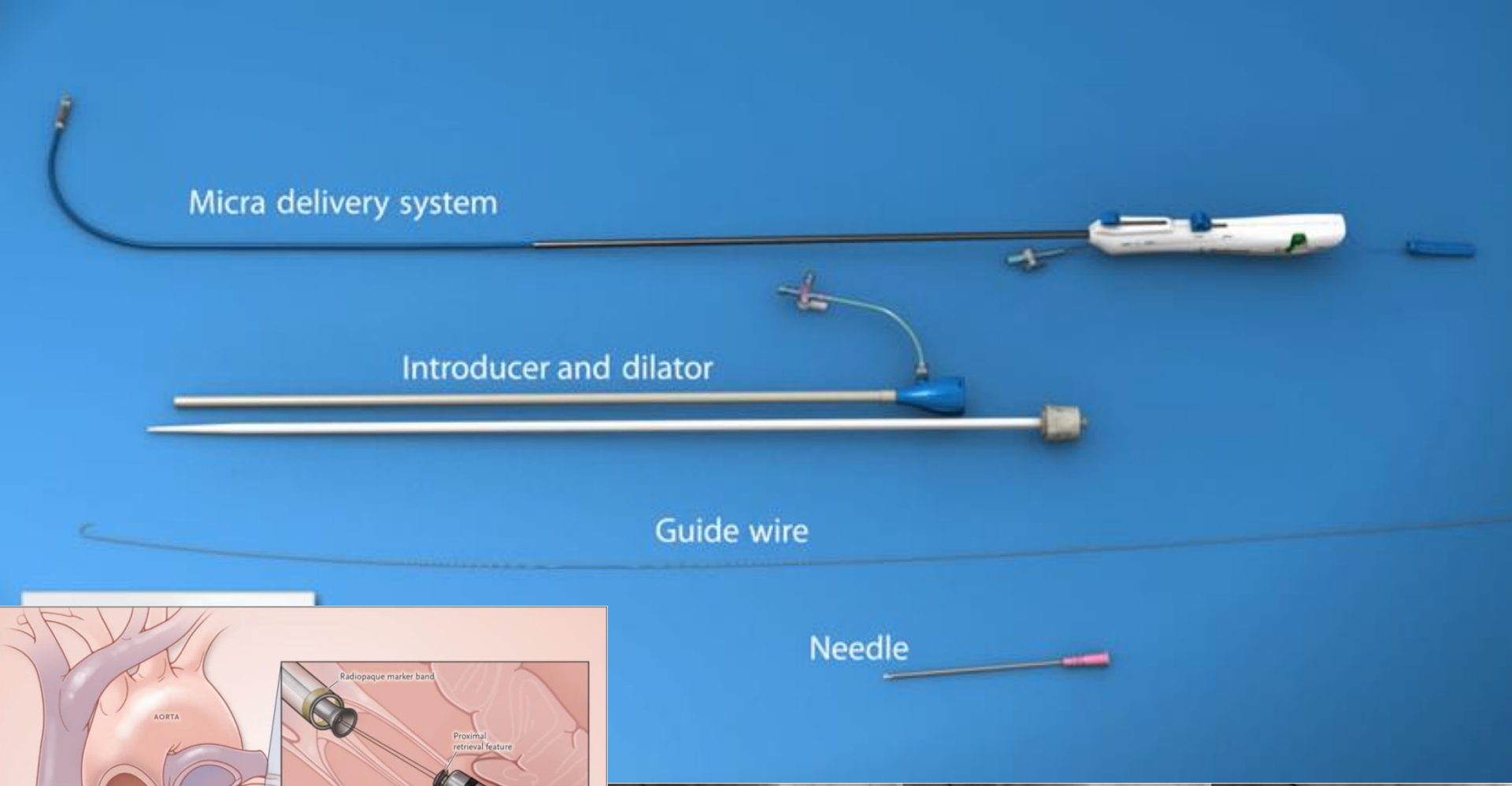


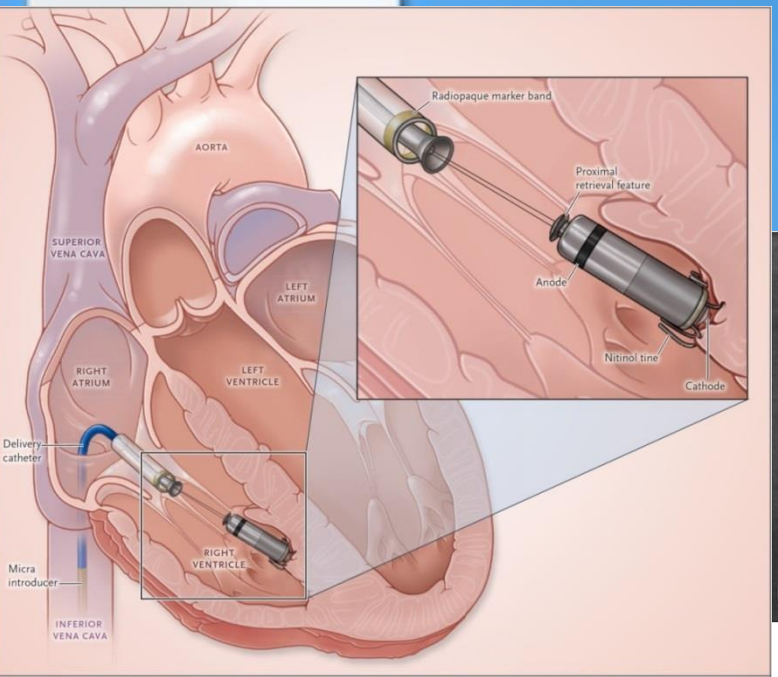
Fig. 8. Nuclear-powered intracardiac pacemaker.

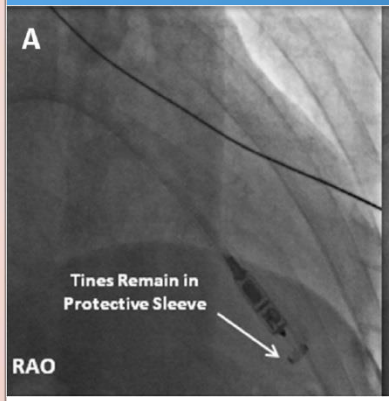


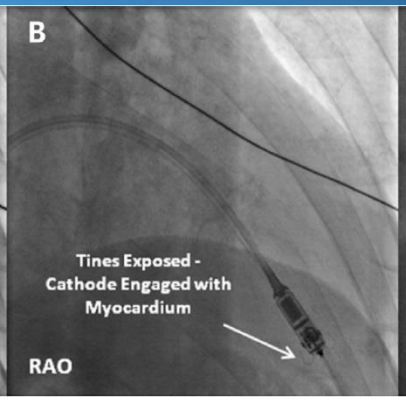


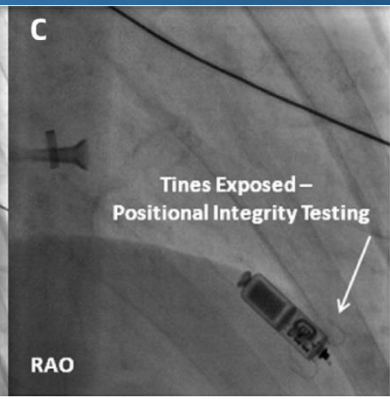
Spickler, J. W., N. S. Rasor, et al. **(1970).** "Totally self-contained intracardiac pacemaker." J Electrocardiol **3**(3-4): 325-331.





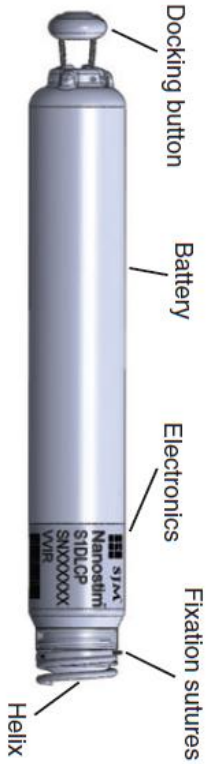






Europace. 2015;17(10):1508-13

State of the art of leadless pacing

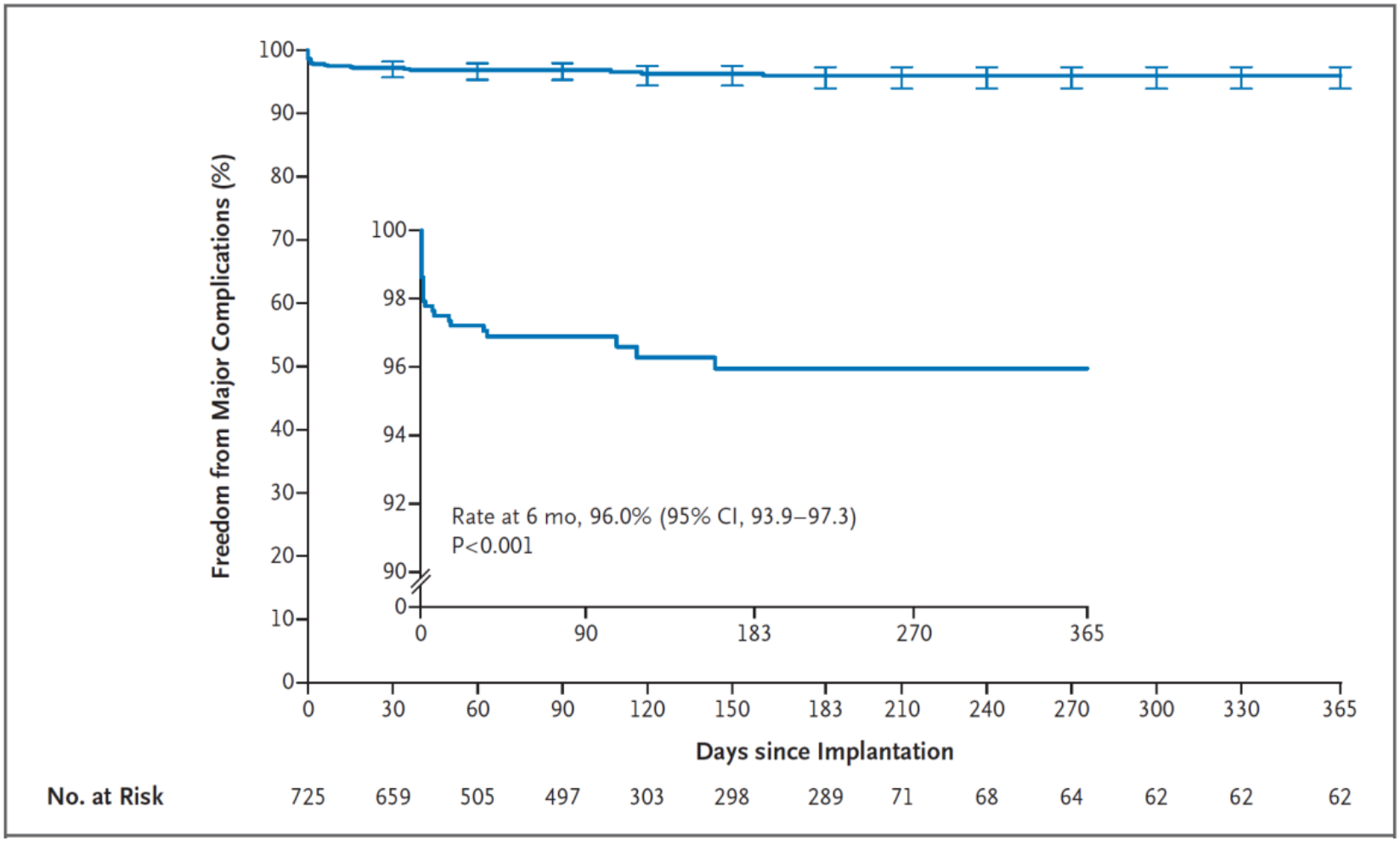


Specificationms	Nanostim™ leadless cardiac pacemaker	Micra™ transcatheter pacing system
Volume (cm^3)	1	0.8
Length (mm)	41.4	25.9
Weight (g)	2	2
Introducer size (French)	18	23
Primary fixation mechanism	Screw-in helix	Self-expanding nitinol tines
Secondary fixation mechanism	Nylon tines	
Pacing mode	VVI/VVIR	VVI/VVIR
Rate response sensor	Temperature	Accelerometer
Energy supply	Integrated battery	Integrated battery
Battery	Lithium carbon-monofluoride	Lithium silver vanadium oxide/carbon monoflouride
Battery longevity (years)	9.8 100%/2.5 V/0.4 ms/ 60b.p.m.	10 100%/1.5 V/ 0.24 ms/ 60 b.p.m.
Device retrieval option	Yes	Yes
Telemetry	Conductive	Radio frequency

Europace. 2015;17(10):1508-13

Leadless pacemaker

Implants rate success Feasibility – safety Complication rate



N Engl J Med 2015; 373:1125-1135

Leadless pacemaker

Implants rate success Feasibility – safety Complication rate

Table 2. Major Complications in 725 Patients Who Underwent a Transcatheter Pacemaker Implantation Attempt.

Adverse Event	No. of Events Associated with Major Complication Criterion*						No. of Patients (%)†
	Death	Loss of Device Function	Hospitalization	Prolonged Hospitalization‡	System Revision	Total Events	
Embolism and thrombosis	0	0	1	1	0	2	2 (0.3)
Deep vein thrombosis	0	0	0	1	0	1	1 (0.1)
Pulmonary thromboembolism	0	0	1	0	0	1	1 (0.1)
Events at groin puncture site: atrioventricular fistula or pseudoaneurysm	0	0	2	3	0	5	5 (0.7)
Traumatic cardiac injury: cardiac perforation or effusion	0	0	3	9	0	11	11 (1.6)
Pacing issues: elevated thresholds	0	1	2	1	2	2	2 (0.3)
Other events	1	0	5	4	1	8	8 (1.7)
Acute myocardial infarction	0	0	0	1	0	1	1 (0.1)
Cardiac failure	0	0	3	2	0	3	3 (0.9)
Metabolic acidosis	1	0	0	0	0	1	1 (0.1)
Pacemaker syndrome	0	0	1	0	1	1	1 (0.2)
Presyncope	0	0	0	1	0	1	1 (0.1)
Syncope	0	0	1	0	0	1	1 (0.1)
Total	1	1	13	18	3	28	25 (4.0)

N Engl J Med 2015; 373:1125-1135

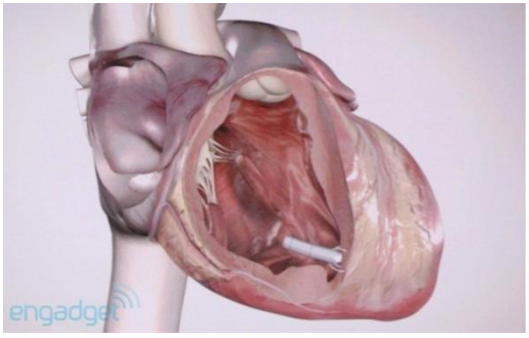
Are Leadless Pacemakers a Niche or the Future of Device Therapy?

Potential advantages

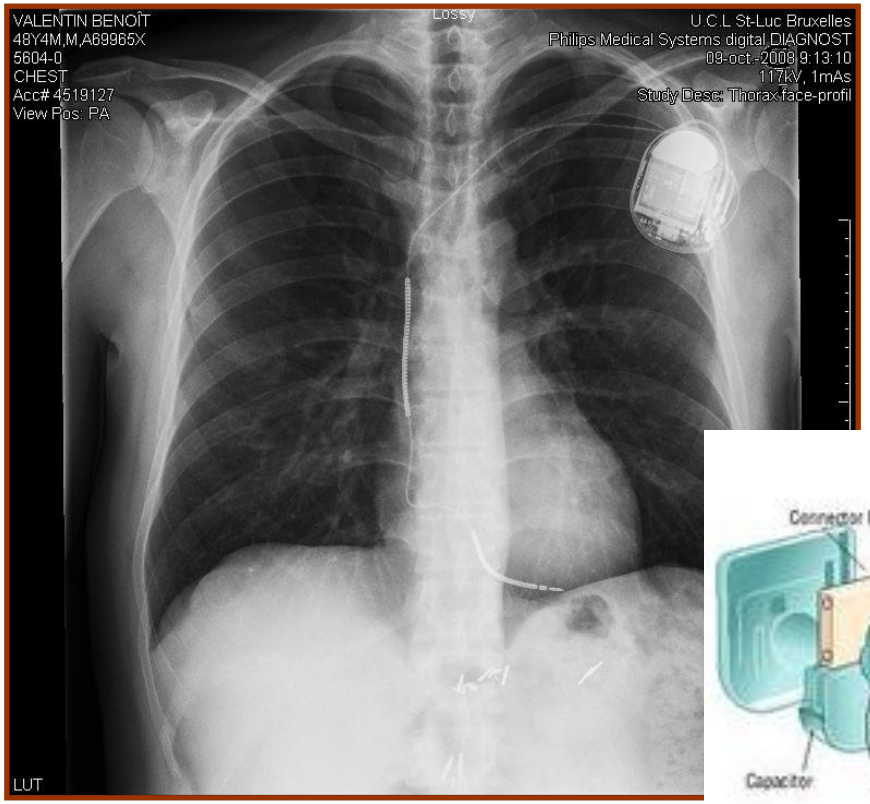
- **Less Invasive**
  - No surgery
  - Fewer complication
  - Less radiation exposure
  - More cosmetic (« invisible)
- **Improved Efficiency**
  - No surgery, less infection risk
  - Femoral venous access
  - No system connections
  - More readily MRI conditional (no antenna)
- **More Cost-Effective**
  - Reduced lengt of hospital day (one day)
  - Fewer acute and chronic complication

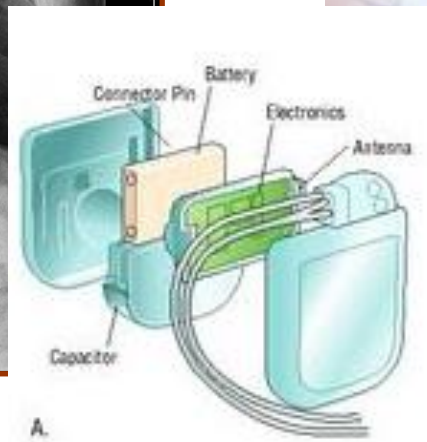
Potential disadvantages

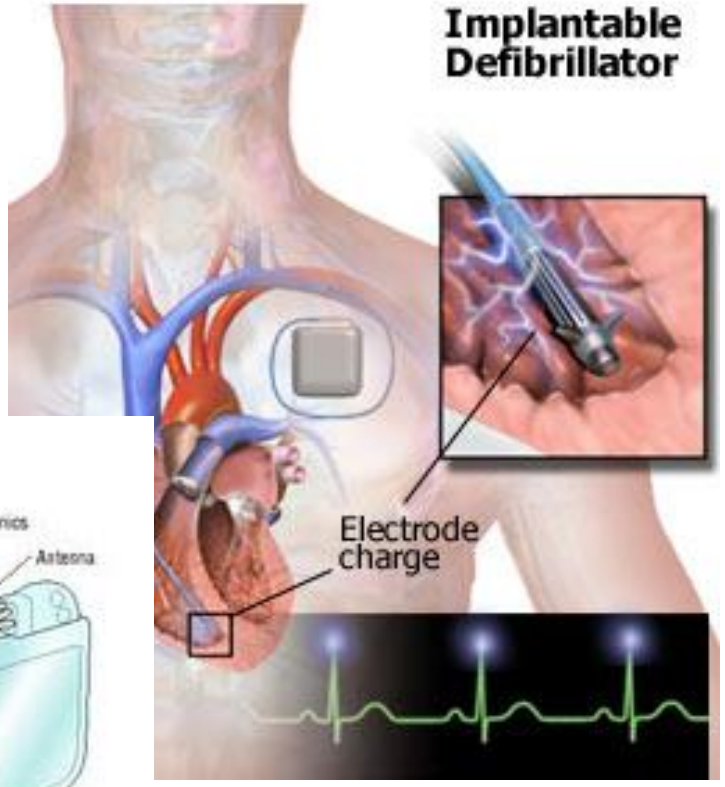
- **Multiple chamber pacing more complex**
  - Wireless communication
  - Memory capacity
- **Implants risk**
  - Large diameter sheaths
  - Embolization/retrieval
  - Repositioning difficulty for high threshold
  - Epicardial access issues
- **Removal/replacement**
  - Longevity limitations
  - Abandon vs explant ?



Human DAI history…







> 2400 DAI en Belgique/an

Castle LW, Cook S: Pacemaker radiography. In Ellenbogen KA, Kay GN, Wilkoff BL [eds]: Clinical Cardiac Pacing. Philadelphia, WB Saunders, 1995, p 538.

Human intracardiac defibrillator history…

CPI Ventak
1555

246g / 145cc

H x W x D:
10.1x 7.6 x 2.0cm

1985

Cadet™ ICD
Model V-105
129g / 73cc

1995

1er modèle DR

Photon™ V-199
85g / 40cc

2001

1er modèle HF

Atlas™
76g / 34cc

2002

Current™
74g / 38cc

2008

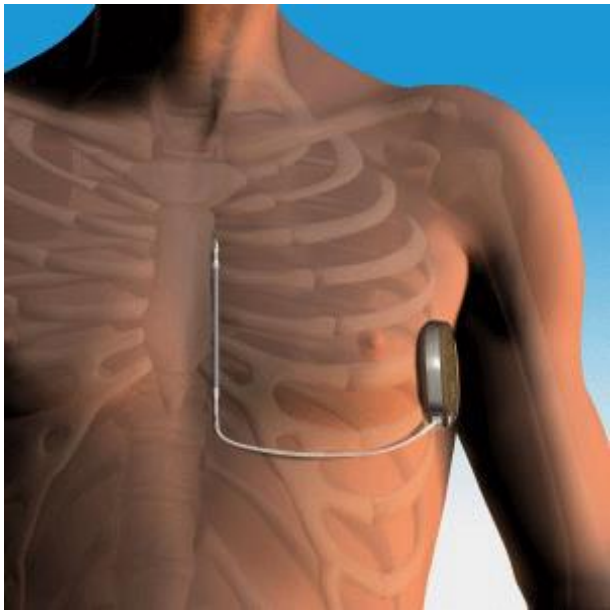
- Heavy surgery
- Abdominal can, epicardial patch
- Non programmable
- Max energy Shock only
- FV only based on frequency
- Criteria > 2 reanimated SCD!
- Longevity : 1 ½ Y

- Local anesthesia
- Venous acces
- Fully programmable
- ATP and shock
- Detection algorythm
- Primary prevention
- Longévité : 5 – 7 Y

Subcutaneous-ICD system

Transvenous ICDs

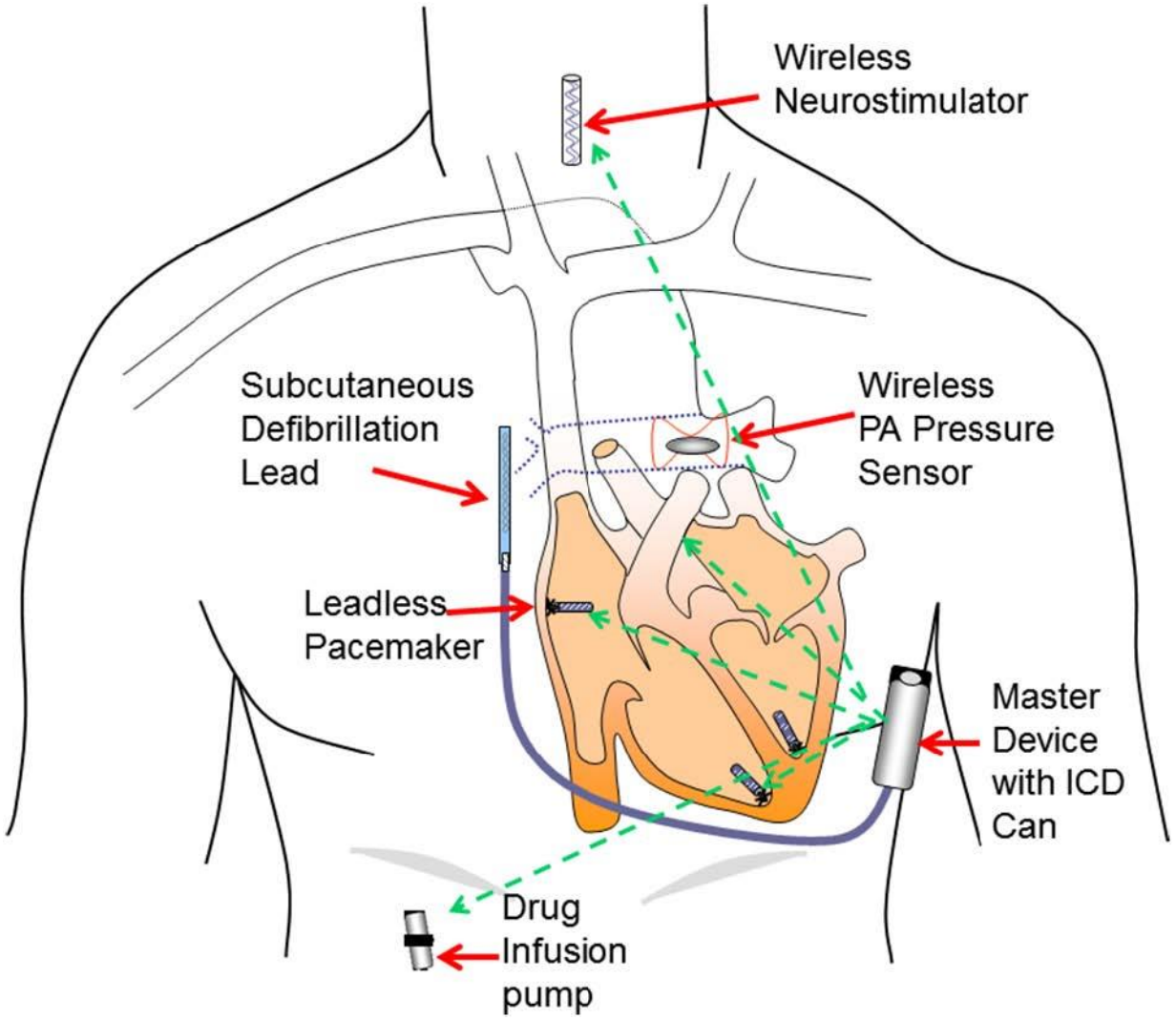
The S-ICD System



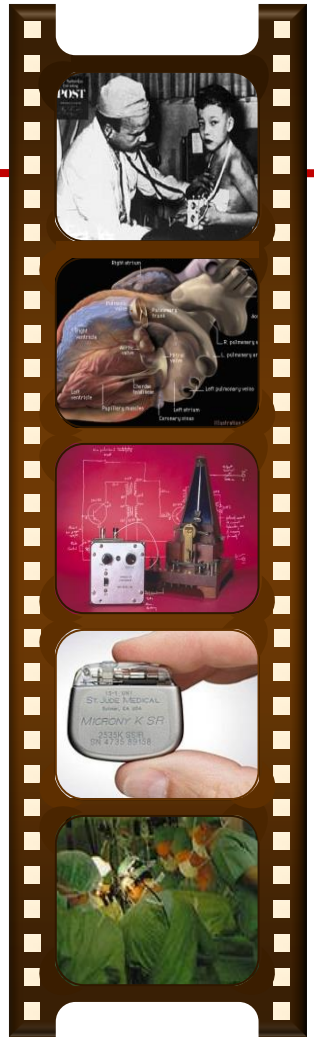
- **Potentiel advantages**
  - Venous system
  - Timing, faster procedure
  - less complication

- **Potentiel disavantages**
  - Size
  - No pacing
  - No ATP
  - Pocket pacing

Futuristic Implantable Device for Cardiac Rhythm Management

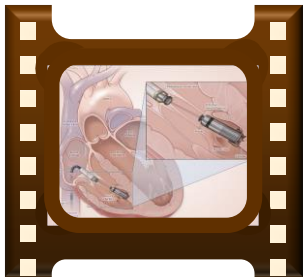


Trends Cardiovasc Med. 2015;25:661-73



Plan

- Introduction
- Nouveautés pharmacologiques
  - Vernakalant
  - Edoxaban
  - Antagoniste NOAC
    - Praxbind
    - Andexanet Alfa
- Nouveautés en stimulation cardiaque
  - Leadless-pacemaker
  - S-ICD
- **Nouveautés en électrophysiologie invasive**
  - Guidelines 2016 ablation FA

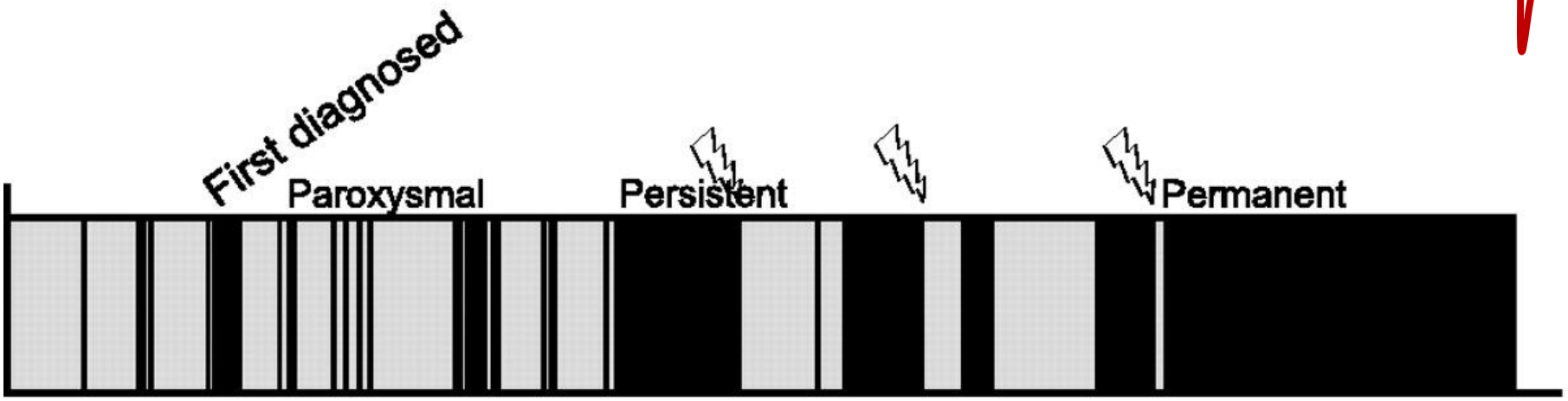


Recommendations for catheter ablation of atrial fibrillation and atrial fibrillation surgery

Recommendations	Class[a]	Level[b]	Ref[c]
Catheter ablation of symptomatic paroxysmal AF is recommended to improve AF symptoms in patients who have symptomatic recurrences of AF on antiarrhythmic drug therapy (amiodarone, dronedarone, flecainide, propafenone, sotalol) and who prefer further rhythm control therapy, when performed by an electrophysiologist who has received appropriate training and is performing the procedure in an experienced centre.	I	A	585–587, 713, 727
Ablation of common atrial flutter should be considered to prevent recurrent flutter as part of an AF ablation procedure if documented or occurring during the AF ablation.	IIa	B	827
Catheter ablation of AF should be considered as first-line therapy to prevent recurrent AF and to improve symptoms in selected patients with symptomatic paroxysmal AF as an alternative to antiarrhythmic drug therapy, considering patient choice, benefit, and risk.	IIa	B	585
All patients should receive oral anticoagulation for at least 8 weeks after catheter (IIaB) or surgical (IIaC) ablation.	IIa	B C	727
Anticoagulation for stroke prevention should be continued indefinitely after apparently successful catheter or surgical ablation of AF in patients at high-risk of stroke.	IIa	C	
When catheter ablation of AF is planned, continuation of oral anticoagulation with a VKA (IIaB) or NOAC (IIaC) should be considered during the procedure, maintaining effective anticoagulation.	IIb	B C	760, 768
Catheter ablation should target isolation of the pulmonary veins using radiofrequency ablation or cryothermy balloon catheters.	IIa	B	585, 715, 716, 734, 735

2016 ESC Guidelines for the management of atrial Fibrillation; EHJ August 2016

Evolution naturelle de la FA



Veines pulmonaires (Trigger)

Ré-entrée fonctionelle (No trigger)

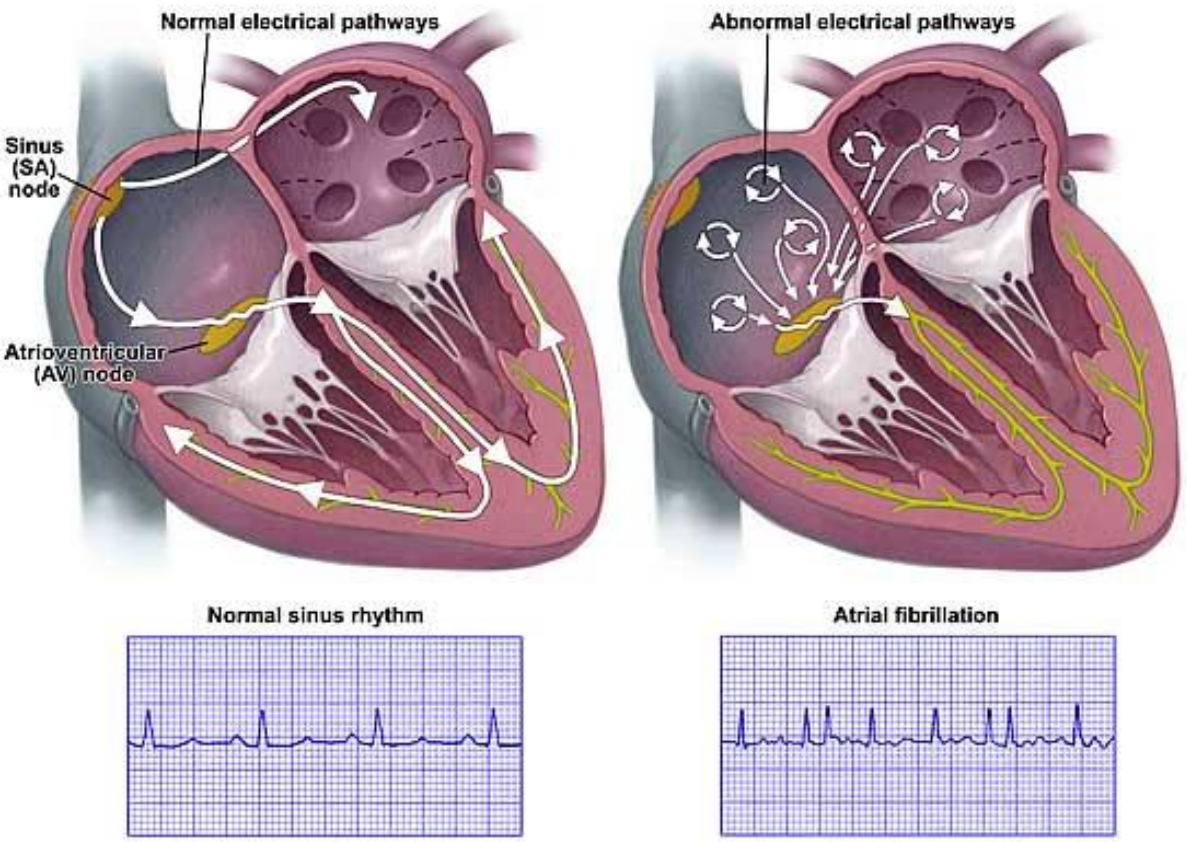
Ré-entrée structurelle (Fibrose)

Probabilité succès ablation

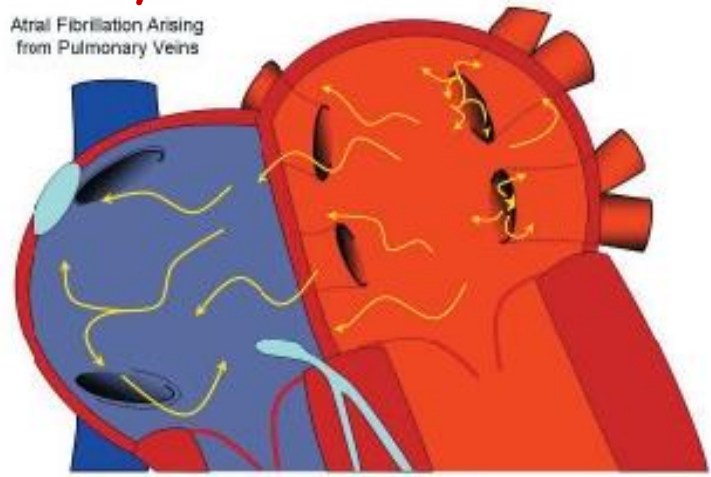
75% **50%** **20%**

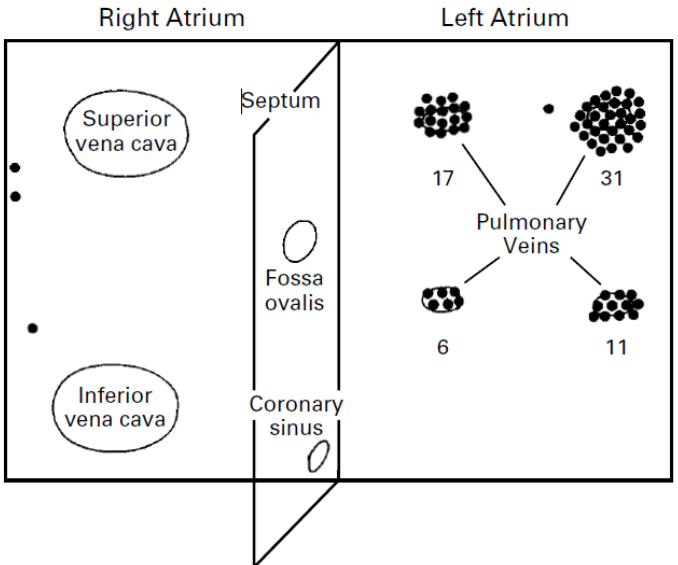
Ablation of Atrial Fibrillation

From Haïssaguerre (1998) …



Paroxysmal atrial fibrillation



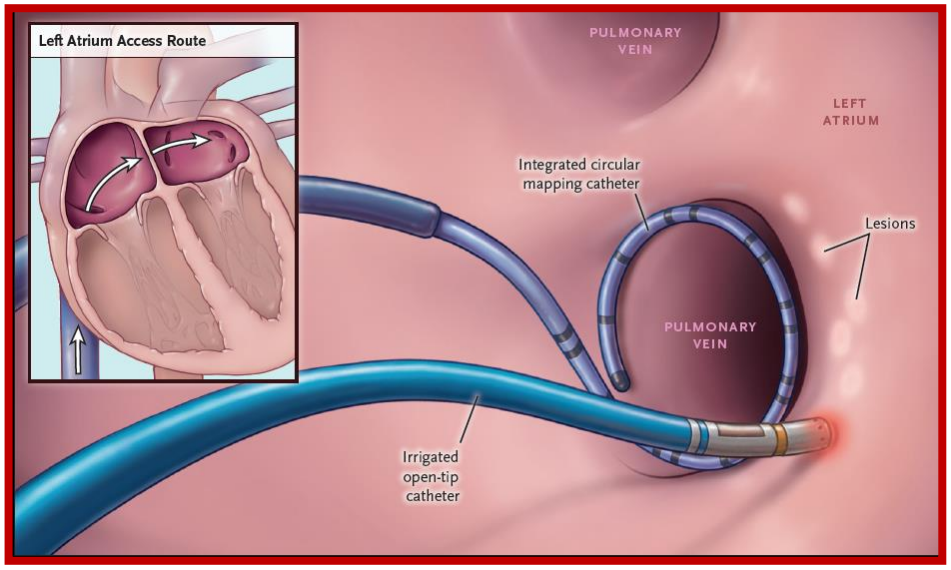


FA: ablation par isolation des veines pulmonaires

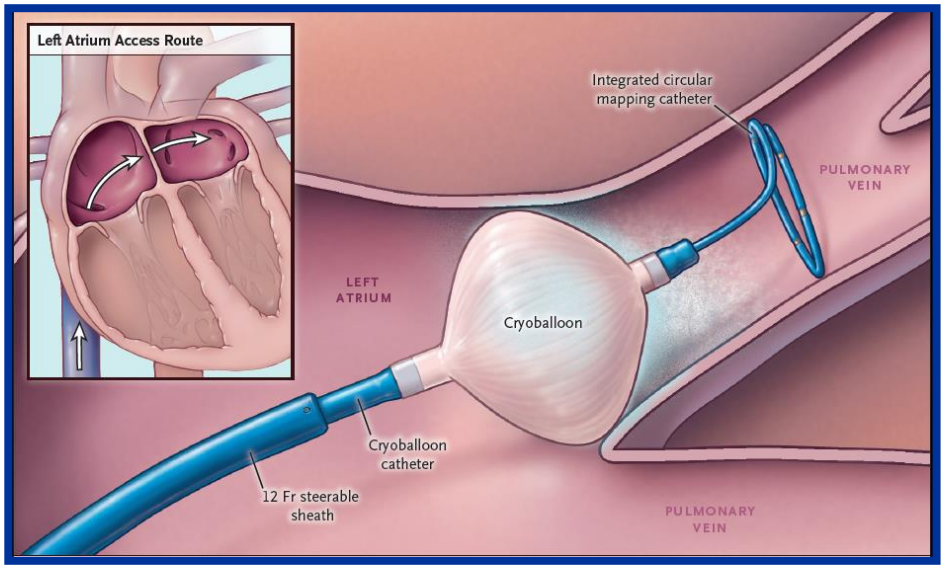
- ***Taux de succès:***
  - FA paroxystique: 70 - 80 %
    - NB: 2 procédures chez 20 à 25 % des patients
  - FA permanente: 50 - 70 % de r. sinusal à 2 ans

- ***Taux complication:*** 1- 2 %
  - AIT/AVC, tamponnade

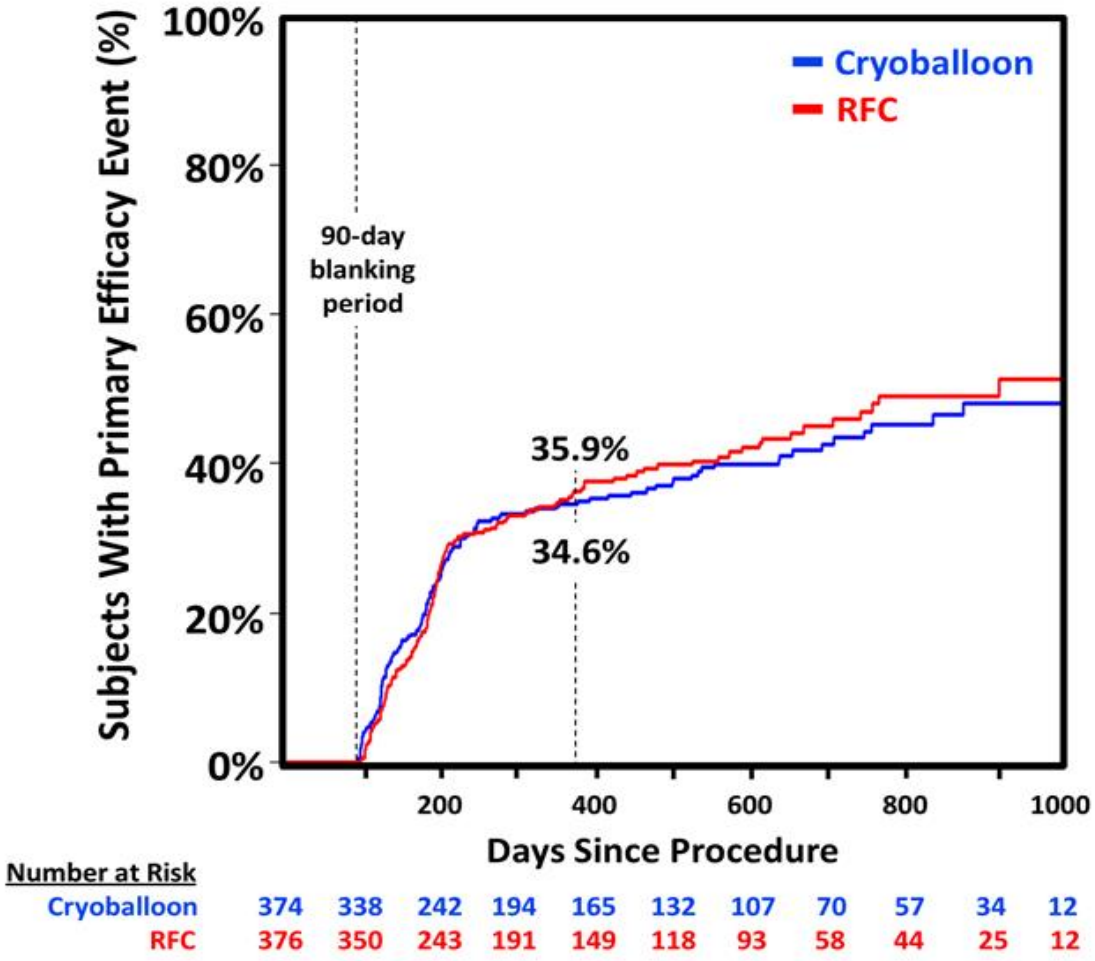
RFC Ablation



Cryoballoon Ablation



Fire and Ice study



Modified ITT analysis

- HR [95% CI] = 0.96 [0.76-1.22]; p = 0.0004
- Non-inferiority hypothesis met
- Superiority test: p = 0.74

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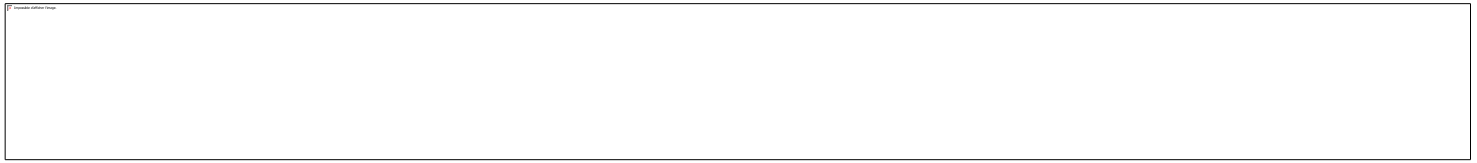
Fire and Ice study



Event (N, %)	RFC (n=376)	Cryoballoon (n=374)
Groin Site Complication*	16 (4.3%)	7 (1.9%)
Atrial Flutter/Atrial Tachycardia**	10 (2.7%)	3 (0.8%)
Phrenic Nerve Injury unresolved at discharge	0	10 (2.7%)***
Unresolved at 3 months	0	2 (0.5%)
Unresolved at > 12 months	0	1 (0.3%)
Cardiac Tamponade/Pericardial Effusion	5 (1.3%)	1 (0.3%)
Stroke/TIA	2 (0.5%)	2 (0.5%)
Atrial Septal Defect	1 (0.3%)	0
Esophageal Ulcer	0	1 (0.3%)
Pericarditis	0	1 (0.3%)
Atrioesophageal Fistula	0	0
Pulmonary Vein Stenosis	0	0

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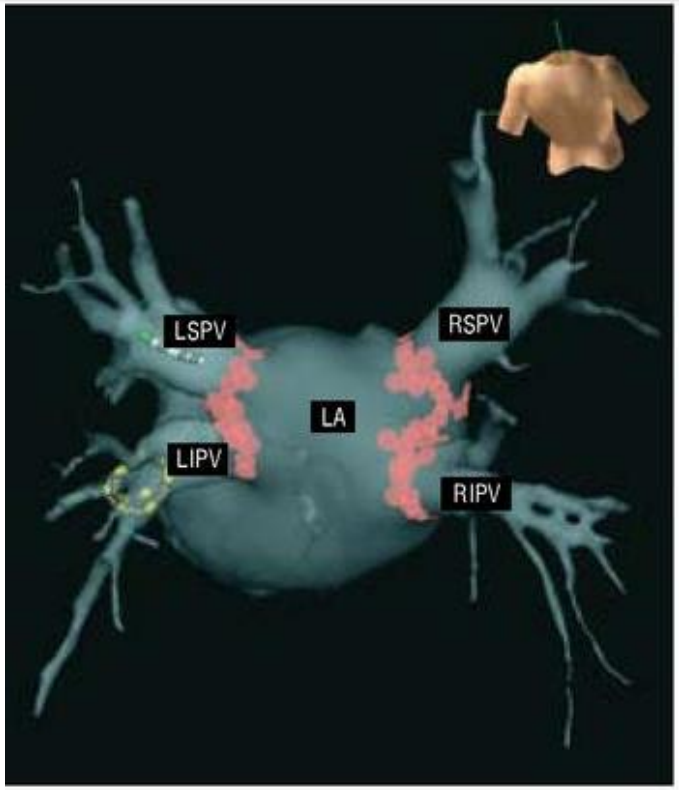
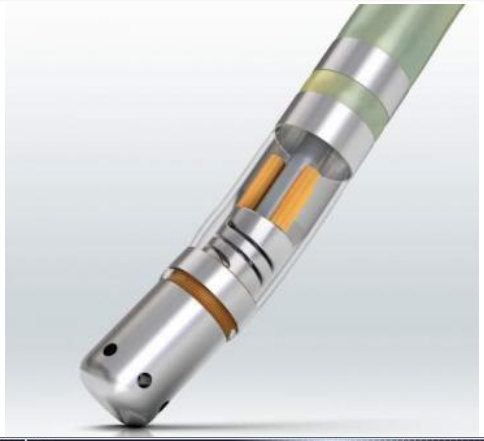
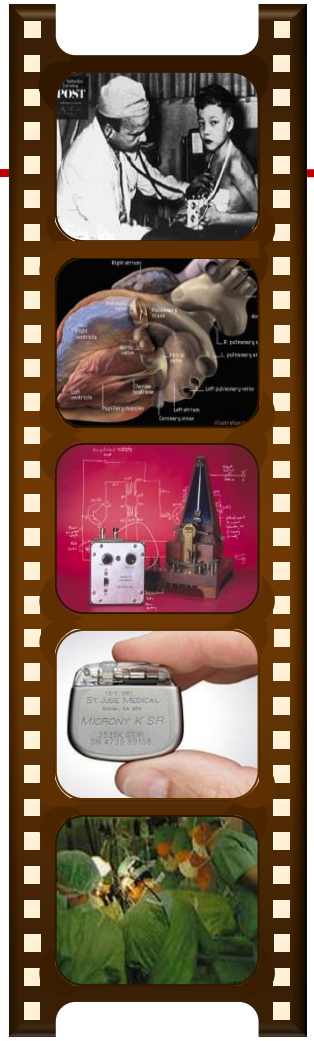
L’ablation de la FA: évolution technologique

Cartographie electro-anatomique



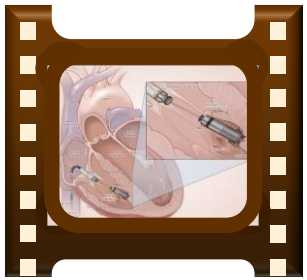
Cathéter contact force





Conclusions

- **Introduction**
- **Nouveautés pharmacologiques**
  - Vernakalant
  - Edoxaban
  - Antagoniste NOAC
    - Praxbind
    - Andexanet Alfa
- **Nouveautés en stimulation cardiaque**
  - Leadless-pacemaker
  - S-ICD
- **Nouveautés en électrophysiologie invasive**
  - Guidelines 2016 ablation FA




Merci !