BIOELECTRICIDAD y MODELADO BIOELÉCTRICO DEL CORAZÓN

Universidad Politécnica de Valencia, España
Universidad Nacional de Lomas de Zamora, Argentina

Prof. José M. Ferrero
Universidad Politécnica de Valencia, España

TEMA 9

SIMULACIÓN COMPUTACIONAL DE ARRITMIAS CARDIACAS

Chema Ferrero

Bioelectricidad y Modelado Computacional del Corazón

TEMA 9

SIMULACIÓN COMPUTACIONAL DE ARRITMIAS CARDIACAS

9.1.- Fundamentos bioeléctricos de las arritmias por reentrada

9.2.- Simulación computacional de arritmias en isquemia miocárdica aguda

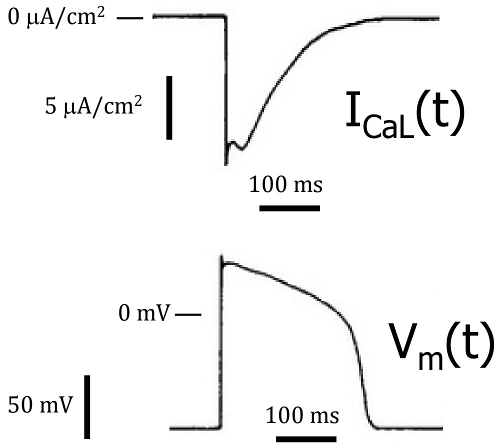
9.3.- Efecto de fármacos en arritmias en isquemia miocárdica aguda

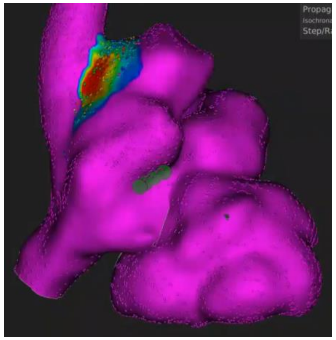
9.4.- Terapia de ablación en infarto crónico

9.5.- Construcción de un modelo cardiaco 3D personalizado a paciente

9.6.- Mejora de la terapia de ablación en pacientes post-infarto mediante simulación

En episodios anteriores…

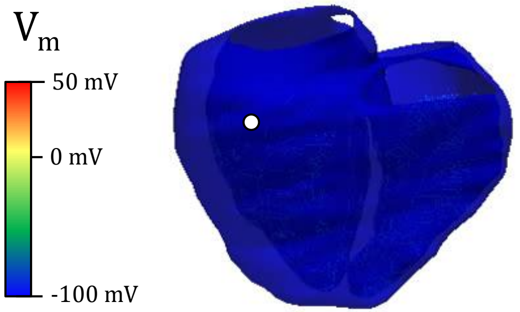




$$p_{oSf} = \prod_i f_{iSf}(t, V_m) \qquad f = 1 \ldots N_f \qquad i = 1 \ldots N_C$$

$$\frac{df_{iSf}}{dt} = \frac{f_{iSf,\infty}(V_m) - f_{iSf}(t)}{\tau_{iSf}(V_m)} \qquad i = 1 \ldots N_C$$

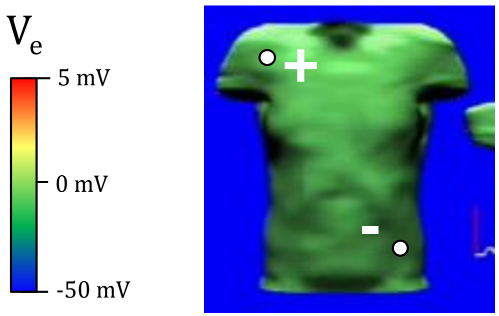
$$E_S = \frac{RT}{z_S F} \ln \frac{[S]_e}{[S]_i} \qquad S = Na^+, Ca^{2+}, K^+, Cl^-$$

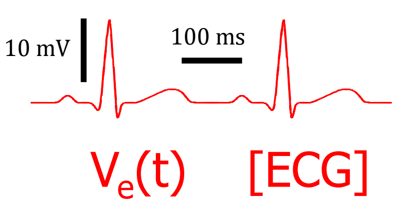


ECUACIONES DEL MODELO BIDOMINIO

$$\boxed{\beta \vec{\nabla} \cdot (\sigma_i \vec{\nabla} V_m) = C_m \frac{\partial V_m}{\partial t} + \sum_f \bar{G}_{Sf}\, p_{oSf} (V_m - E_S) + \sum_{b,i} I_{b,i} + I_{est}}$$

Ecuación de la propagación



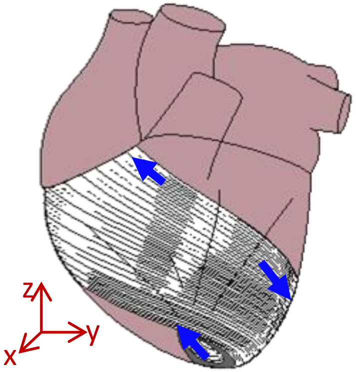


$$\boxed{(1+\lambda)\, \vec{\nabla} \cdot (\sigma_e \vec{\nabla} V_e) = -\vec{\nabla} \cdot (\sigma_i \vec{\nabla} V_m)}$$

Ecuación del Potencial Extracelular

$$\bar{\bar{\sigma}}_e = \lambda \bar{\bar{\sigma}}_i \qquad \beta = \frac{1}{(1+\lambda) S_V}$$

En episodios anteriores…



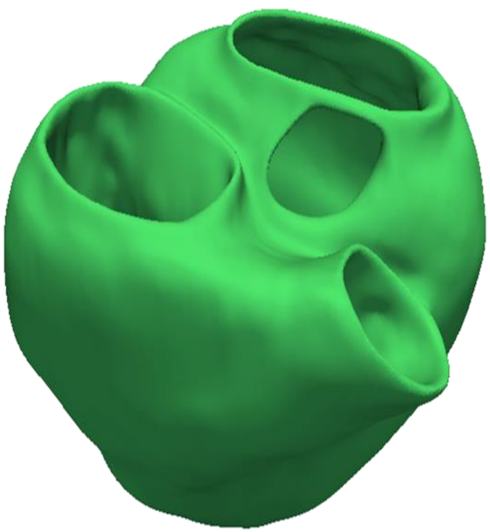
$$\beta \vec{\nabla}\cdot(\sigma_i \vec{\nabla} V_m) = C_m \frac{\partial V_m}{\partial t} + \sum_f \bar{G}_{Sf}\, p_{oSf}\,(V_m - E_S) + \sum_{b,i} I_{b,i} + I_{est}$$

$$p_{oSf} = \prod_i f_{iSf}(t, V_m) \qquad E_S = \frac{RT}{z_S F} \ln \frac{[S]_e}{[S]_i}$$

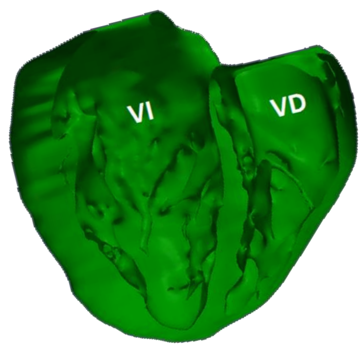
$$\frac{df_{iSf}}{dt} = \frac{f_{iSf,\infty}(V_m) - f_{iSf}(t)}{\tau_{iSf}(V_m)}$$

Epicardio: O'Hara et al., 2011, versión EPI
Midmiocardio: O'Hara et al., 2011, versión MID
Endocardio: O'Hara et al., 2011, versión ENDO
Purkinje: Stewart et al., 2009
Infarto/fibrosis: MacCannel et al., 2007
Isquemia aguda: Gironés-Sangüesa et al., 2020

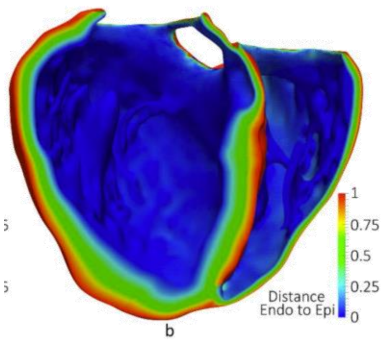
Corazón (ventrículos)



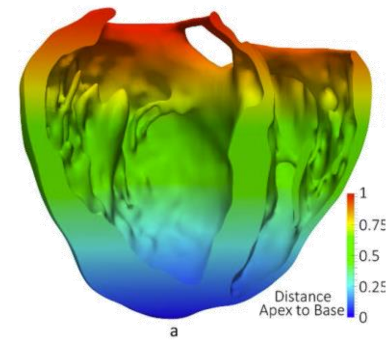
Geometría



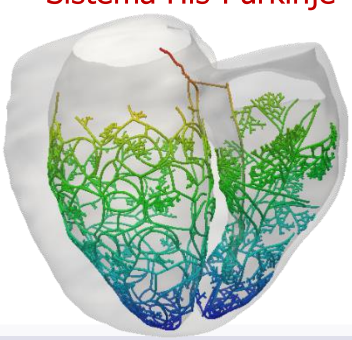
Heterogeneidad transmural



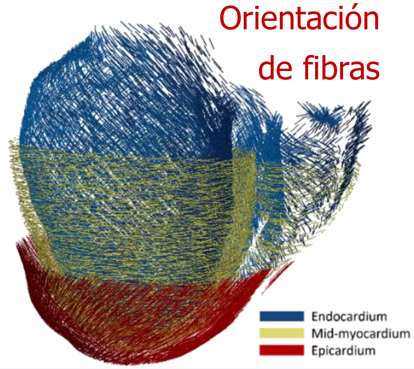
Heterogeneidad ápex-base



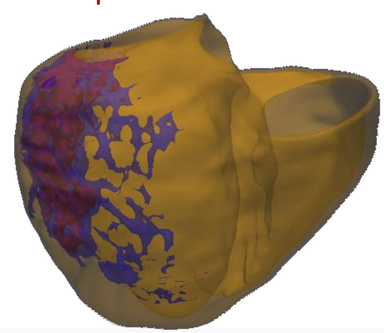
Sistema His-Purkinje



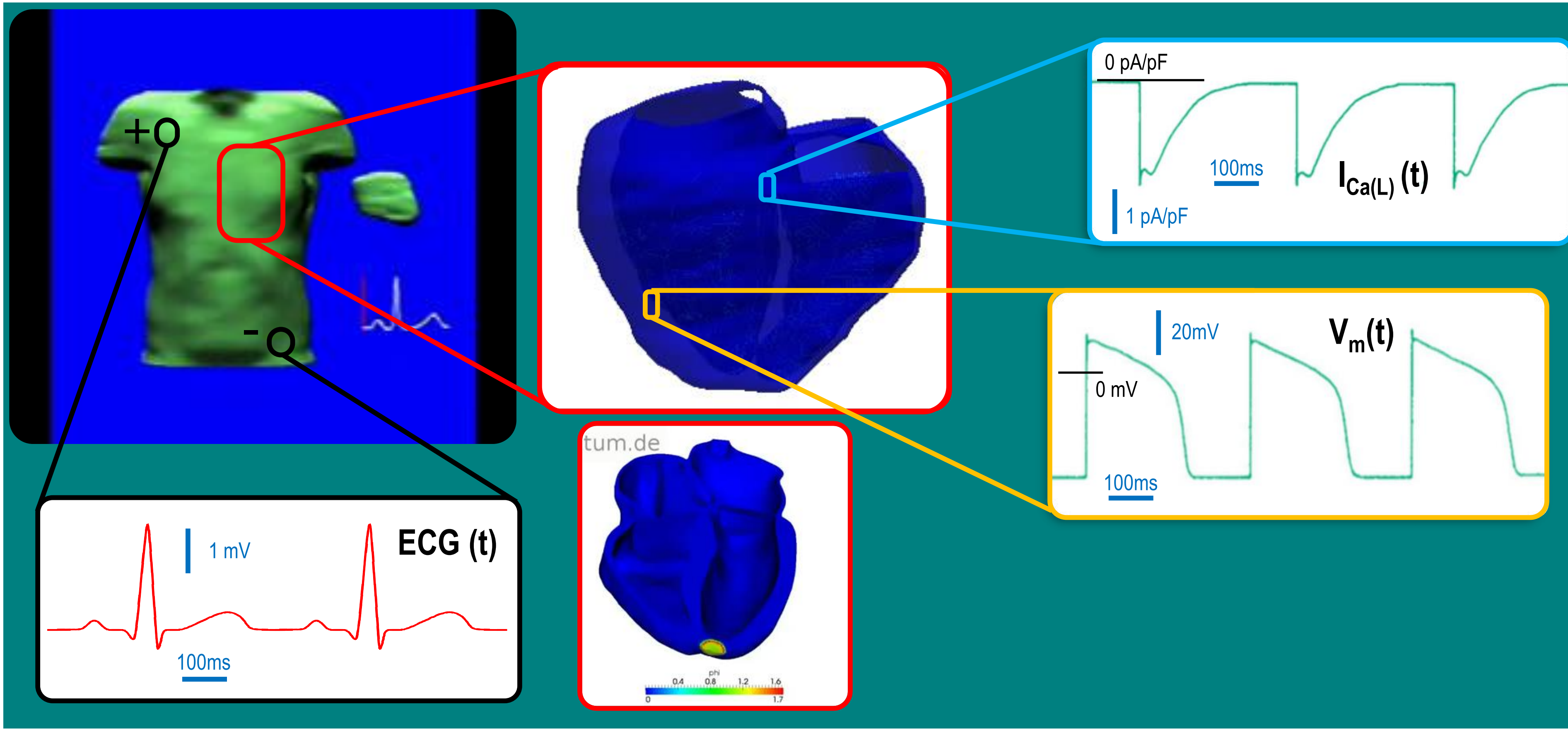
Orientación de fibras



Isquemia o infarto



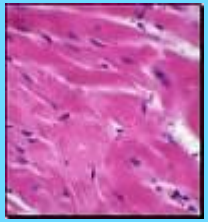
Multiscale cardiac simulations



Body

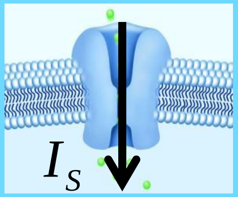
Organ

Tissue



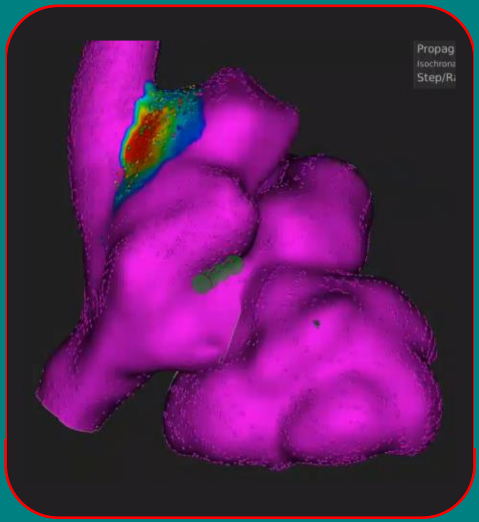
Cell

Ion channel



Multiscale cardiac simulations

experimental



[A. Ferrero et al., 2017]

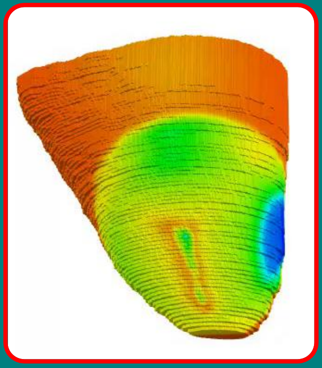
simulation

[Ch Ferrero et al., 2016]

NORMAL

"sinus rhythm"

simulation



[Heidenreich et al., 2011]

experimental

[Gray et al., 1995]

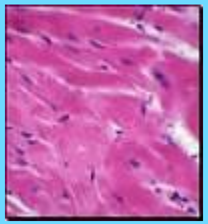
ABNORMAL

"reentry"

Body

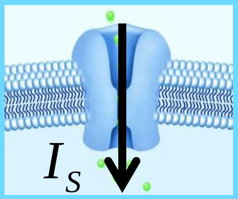
Organ

Tissue



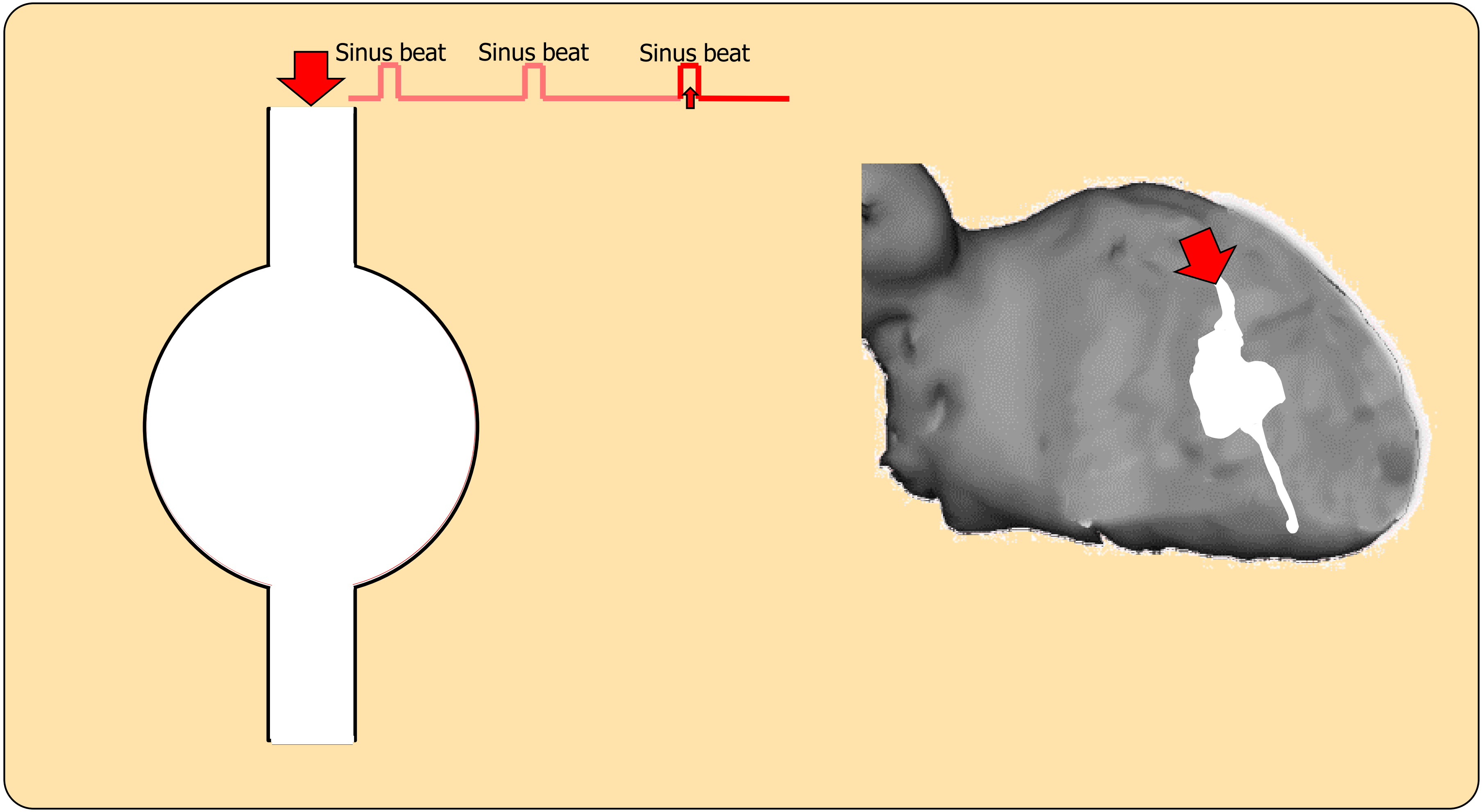
Cell

Ion channel



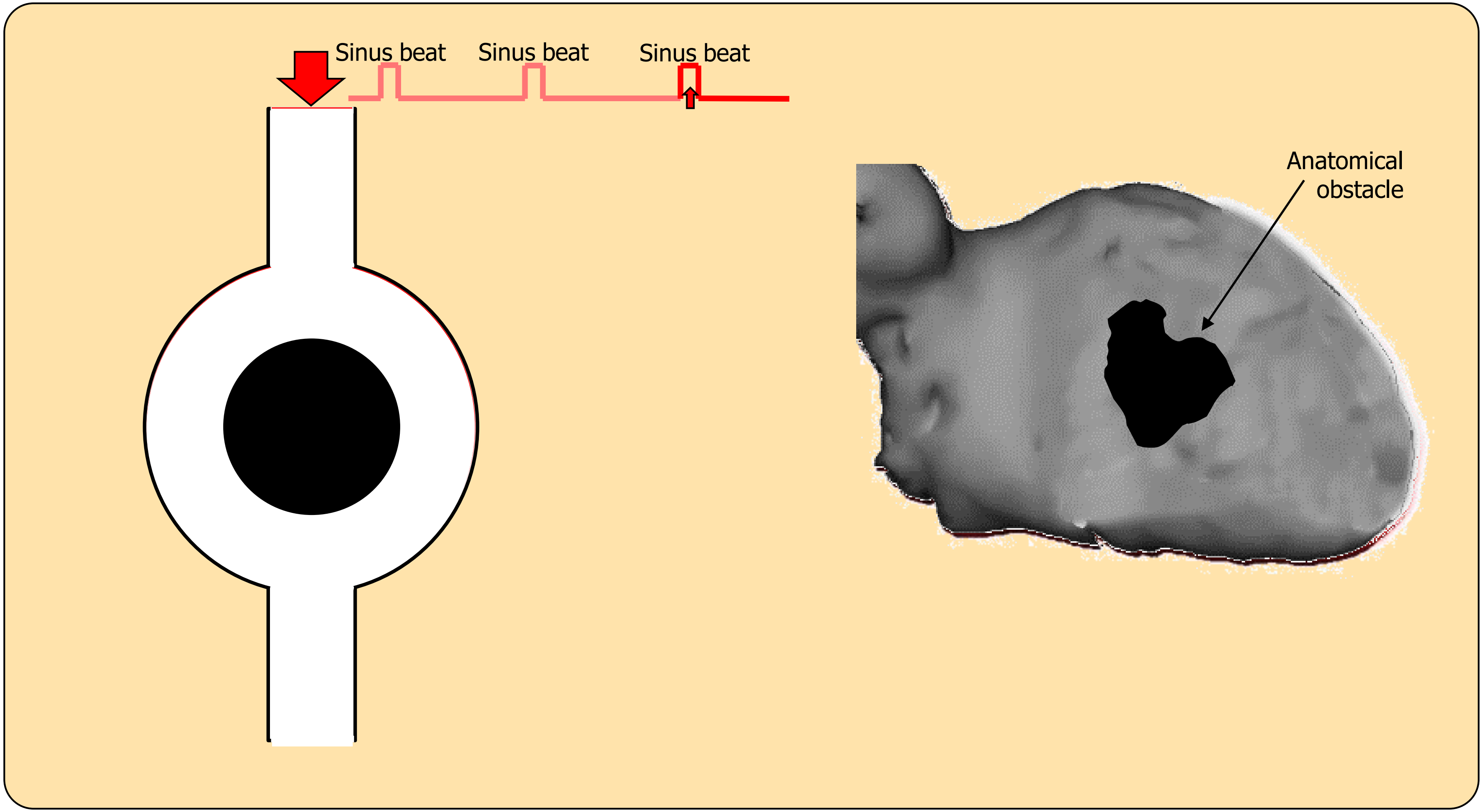
Reentrant Cardiac Arrhythmias

Normal tissue, sinus beats



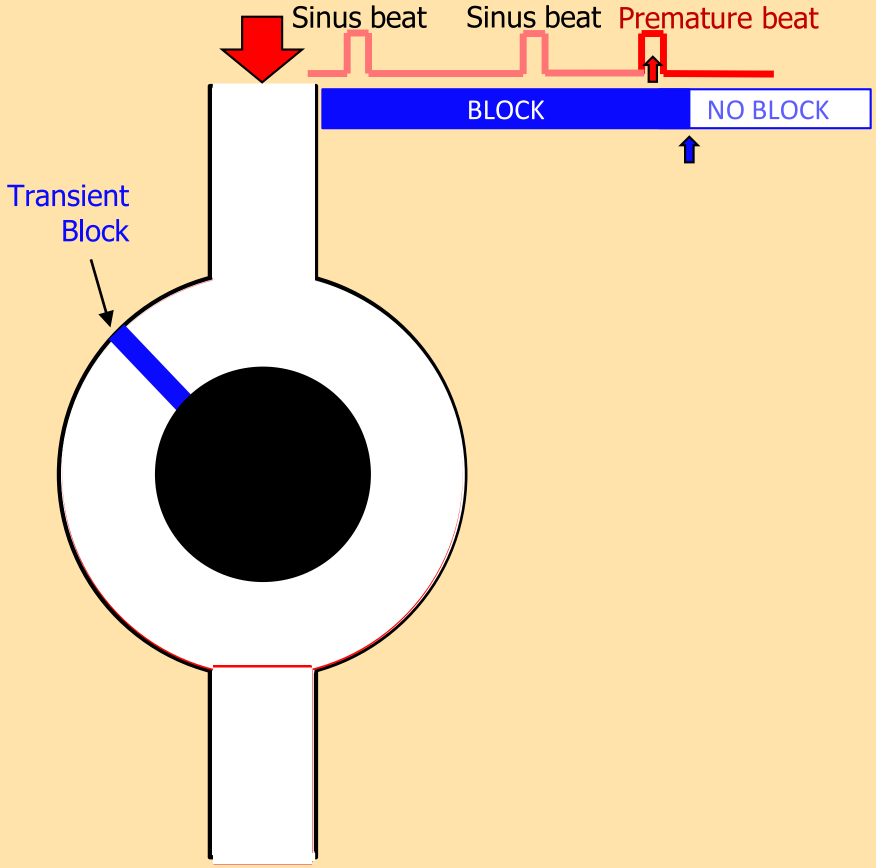
Reentrant Cardiac Arrhythmias

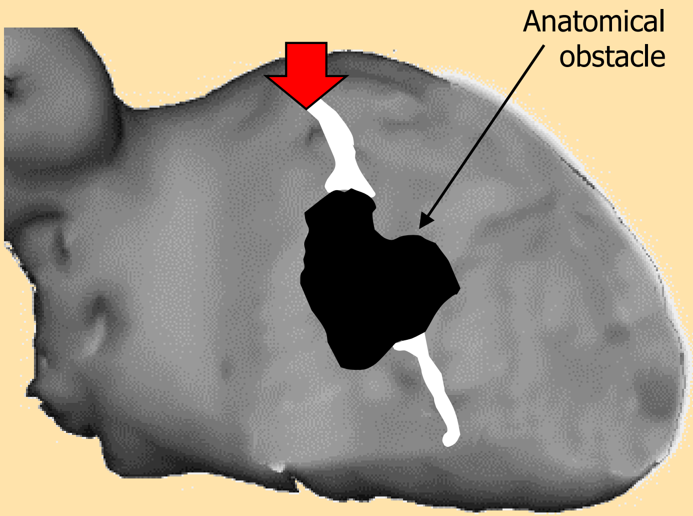
Abnormal tissue (obstacle), sinus beats



Reentrant Cardiac Arrhythmias

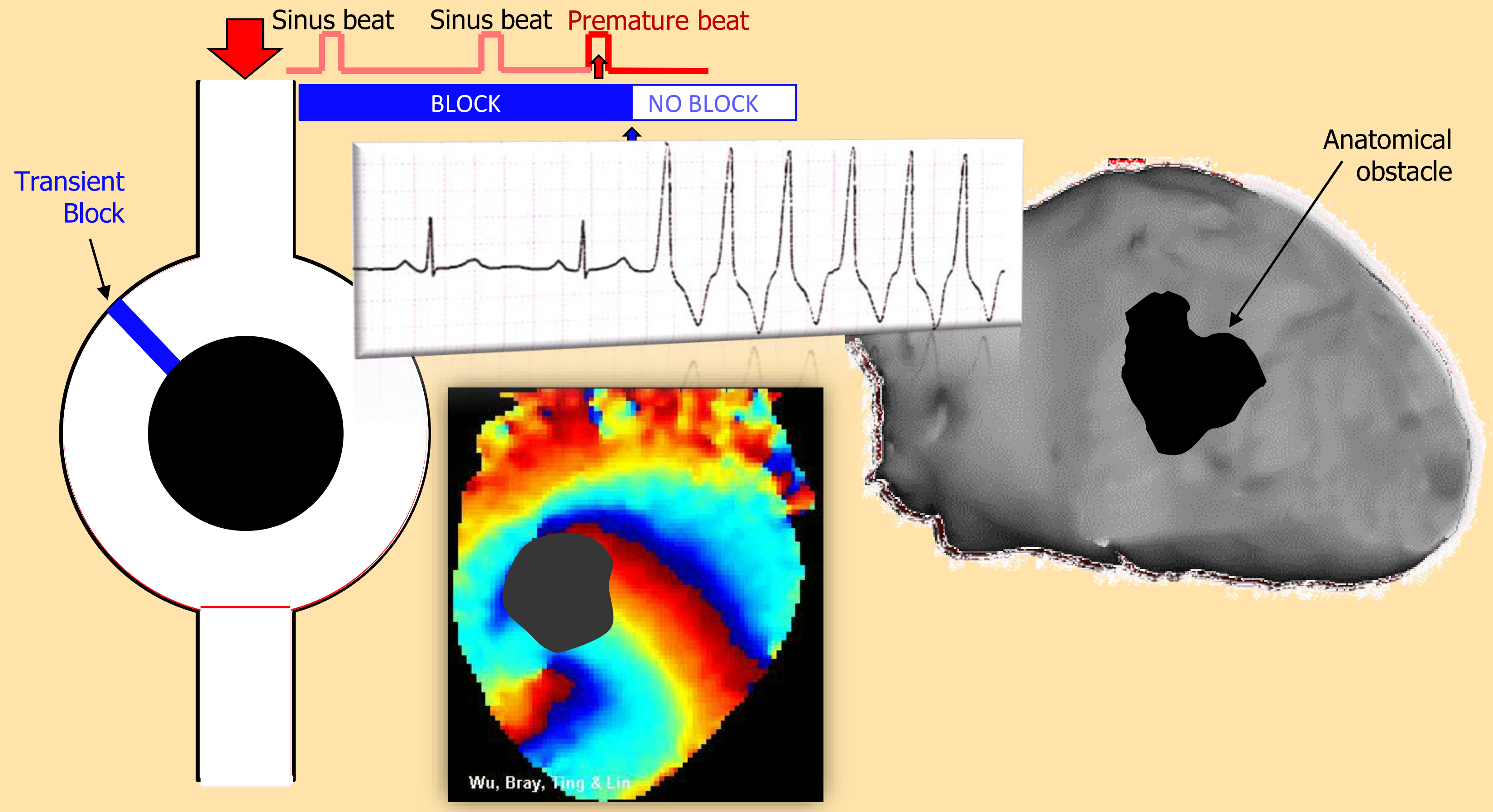
Abnormal tissue (obstacle), premature beat + transient block





Reentrant Cardiac Arrhythmias

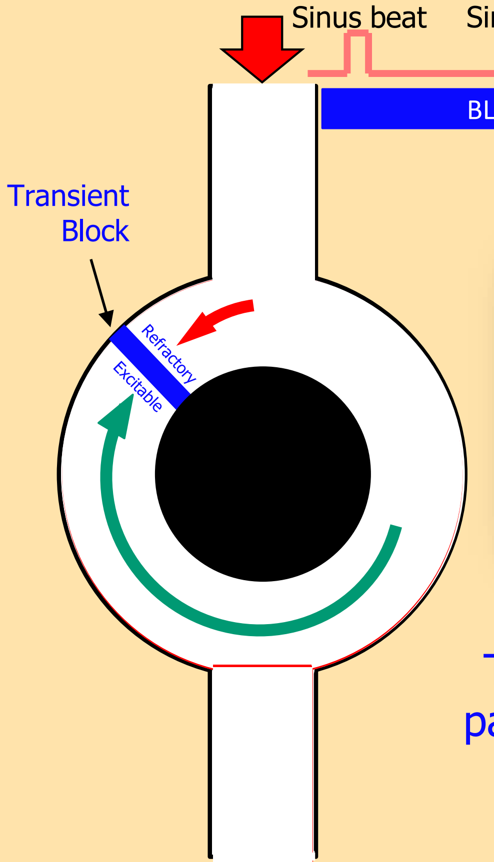
Abnormal tissue (obstacle), premature beat + transient block

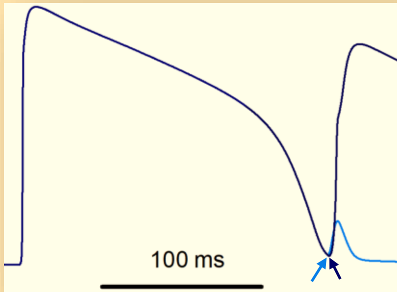


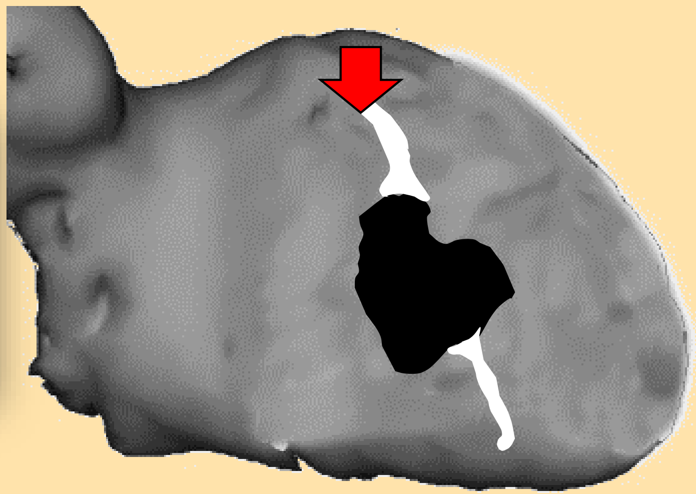
[Wu et al., 2003]

Reentrant Cardiac Arrhythmias

Abnormal tissue (obstacle), premature beat + transient block



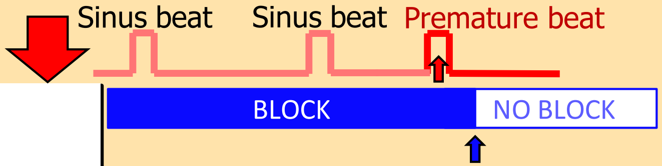


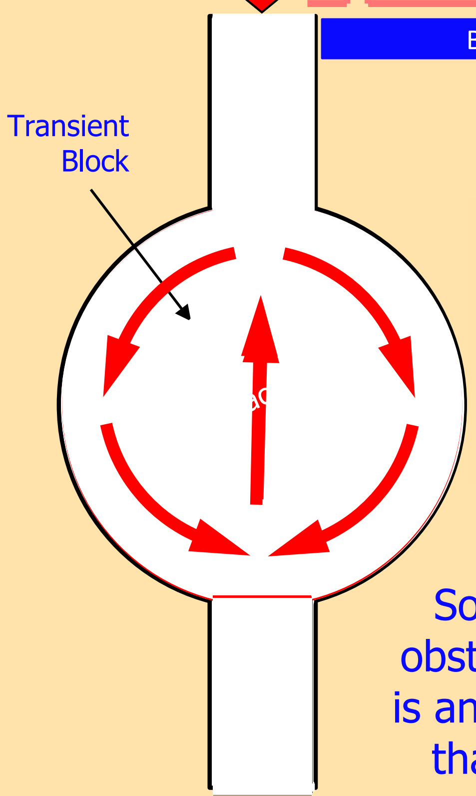


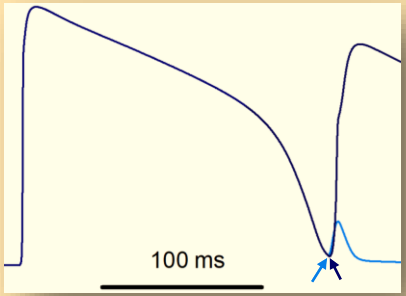
The transient block is usually a part of the myocardium that is in refractory state when the premature wavefront arrives

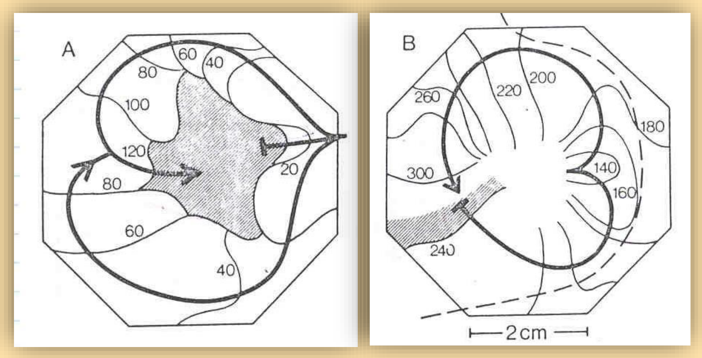
Reentrant Cardiac Arrhythmias

Abnormal tissue (obstacle), premature beat + transient block









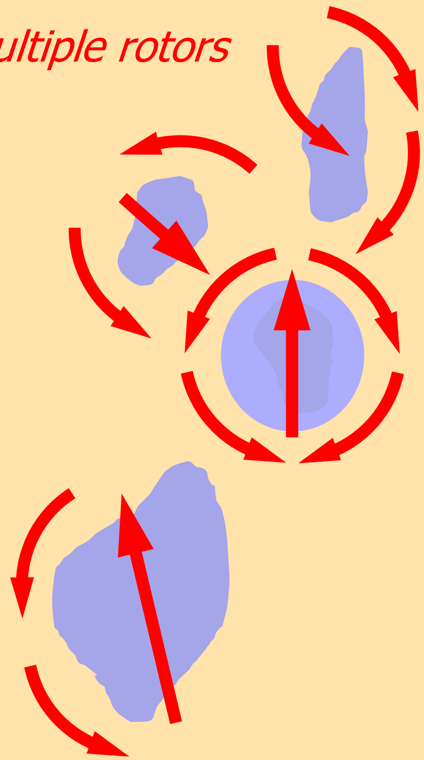
Wit & Janse, 1981

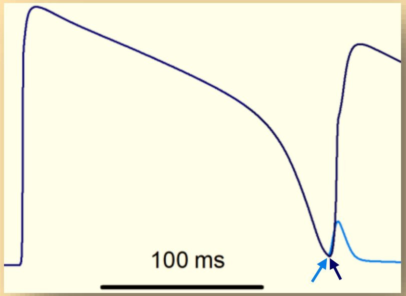
Sometimes, there is no anatomical obstacle but rather the transient block is an extensive part of the myocardium that is in refractory state when the premature wavefront arrives

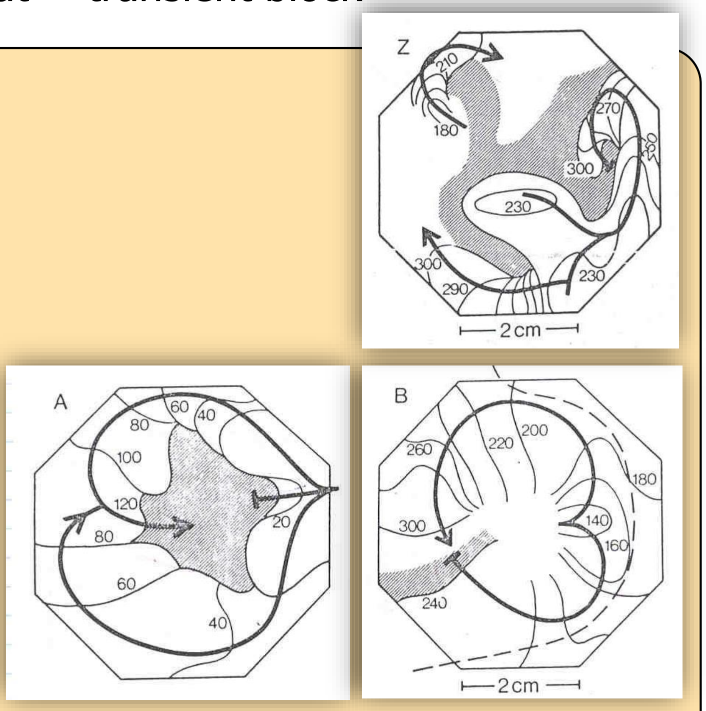
Reentrant Cardiac Arrhythmias

Abnormal tissue (obstacle), premature beat + transient block

Multiple rotors







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Reentrant Cardiac Arrhythmias

Abnormal tissue (obstacle), premature beat + transient block

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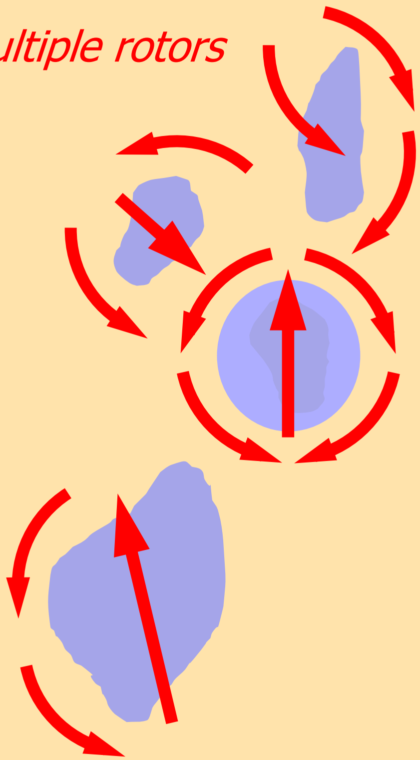
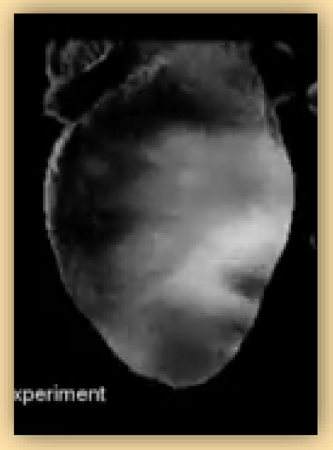
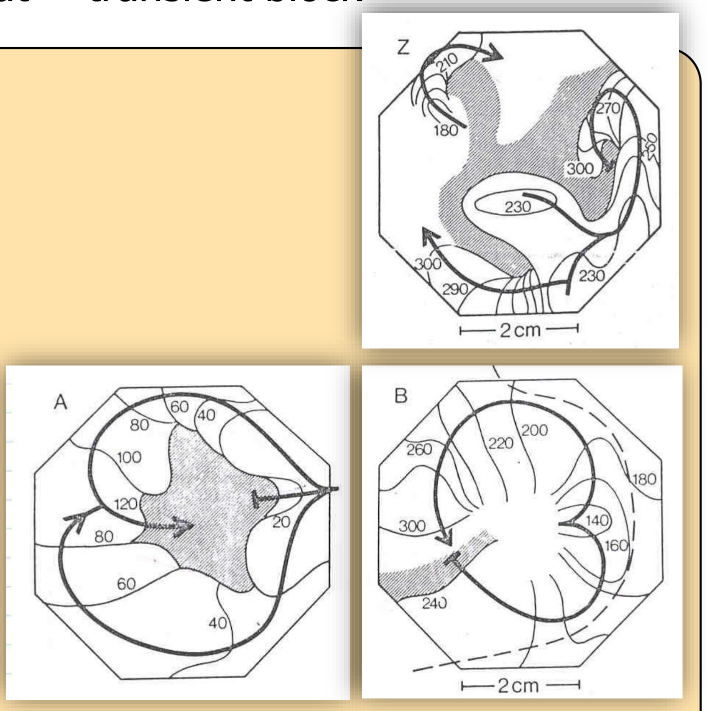


[Gray et al., 1995]

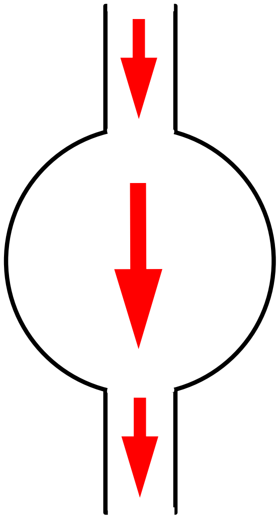




Wit & Janse, 1981

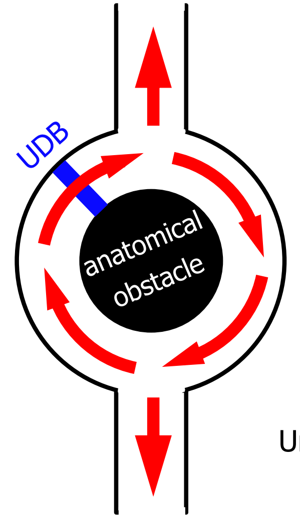
Sometimes, there is no anatomical obstacle but rather the transient block is an extensive part of the myocardium that is in refractory state when the premature wavefront arrives

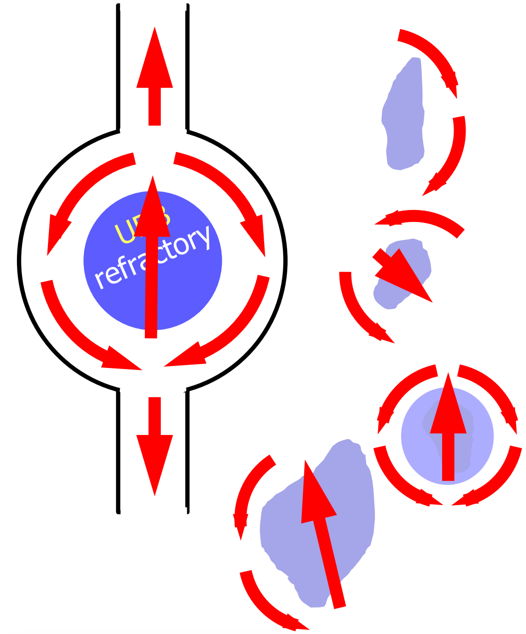
Reentrant Cardiac Arrhythmias: summary



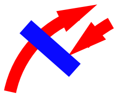
Normal conduction

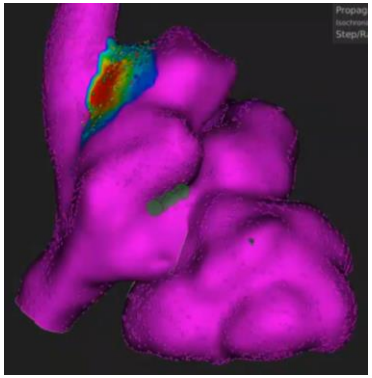
Reentry



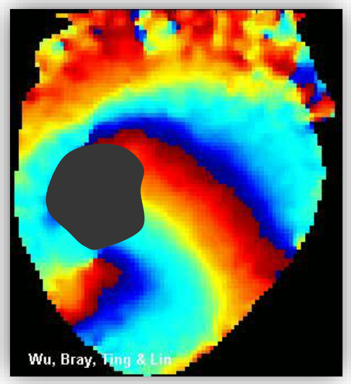


Unidirectional block (UDB)





Sinus rhythm



Ventricular Tachycardia

Ventricular Fibrillation

Tema 9

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CRÉDITOS…

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Duke University, Singapore

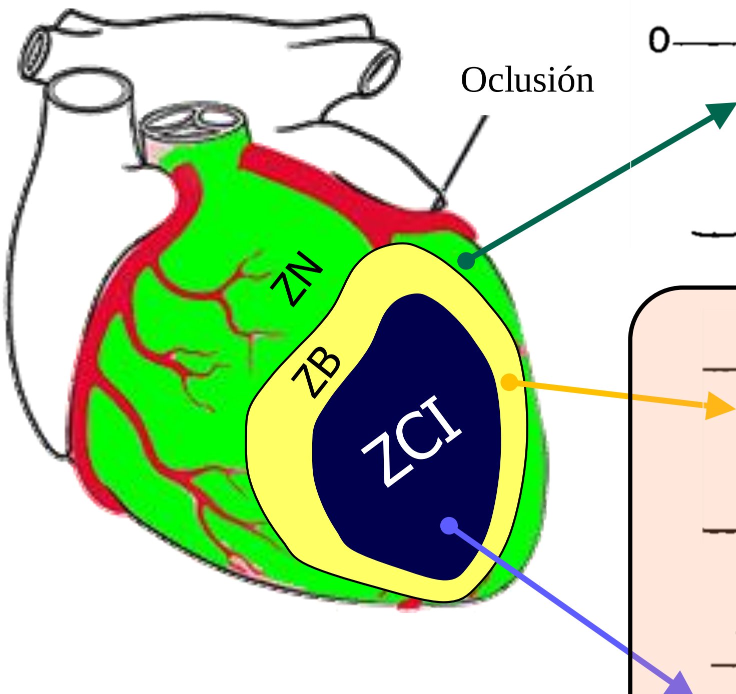
Frank Starmer

Universidad de Zaragoza, España

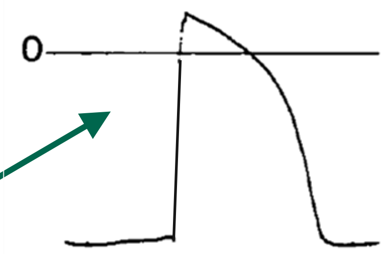
Andrés Mena-Tóbar

Isquemia miocárdica aguda

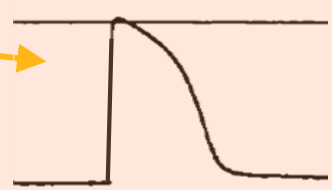
0-30 min: ISQUEMIA AGUDA



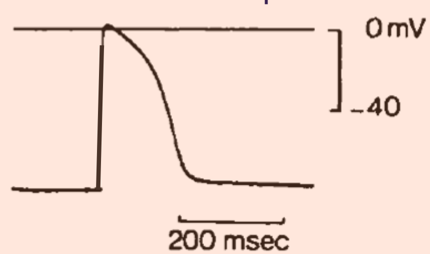
Zona Normal



Zona de Borde



Zona Central Isquémica

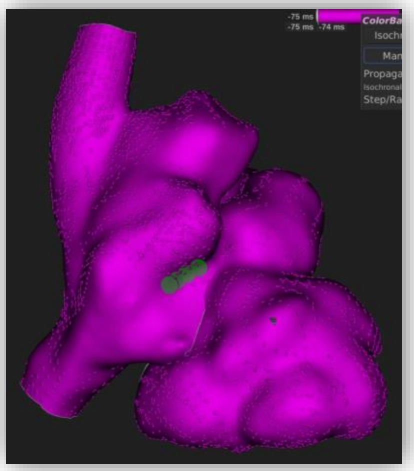


Efecto directo de los cambios metabólicos

ZCI: Zona Central Isquémica
ZB: Zona de Borde
ZN: Zona Normal

(tiempo ÷ 25)

[A Ferrero et al, 2018]



Ritmo Sinusal

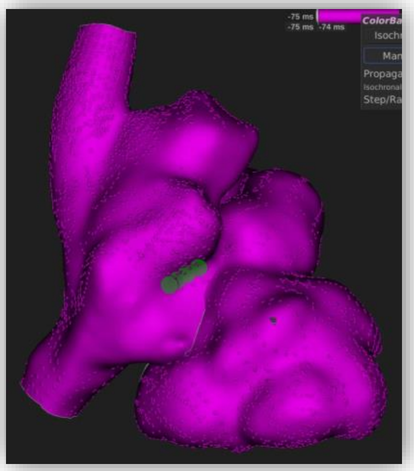
[Gray et al., 1995]

Fibrilación Ventricular

Isquemia miocárdica aguda

(tiempo ÷ 25)

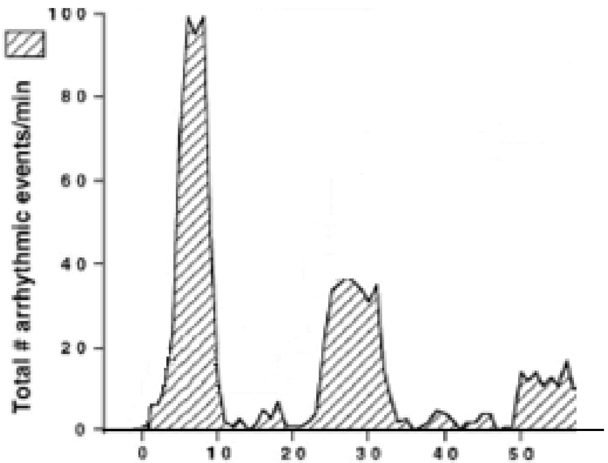
[A Ferrero et al, 2018]



Ritmo Sinusal

7,000,000 de muertes al año

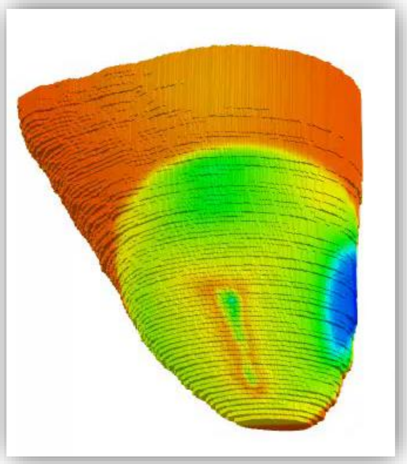
RIESGO DE SUFRIR ARRITMIAS



minutos

[Smith et al,1995]

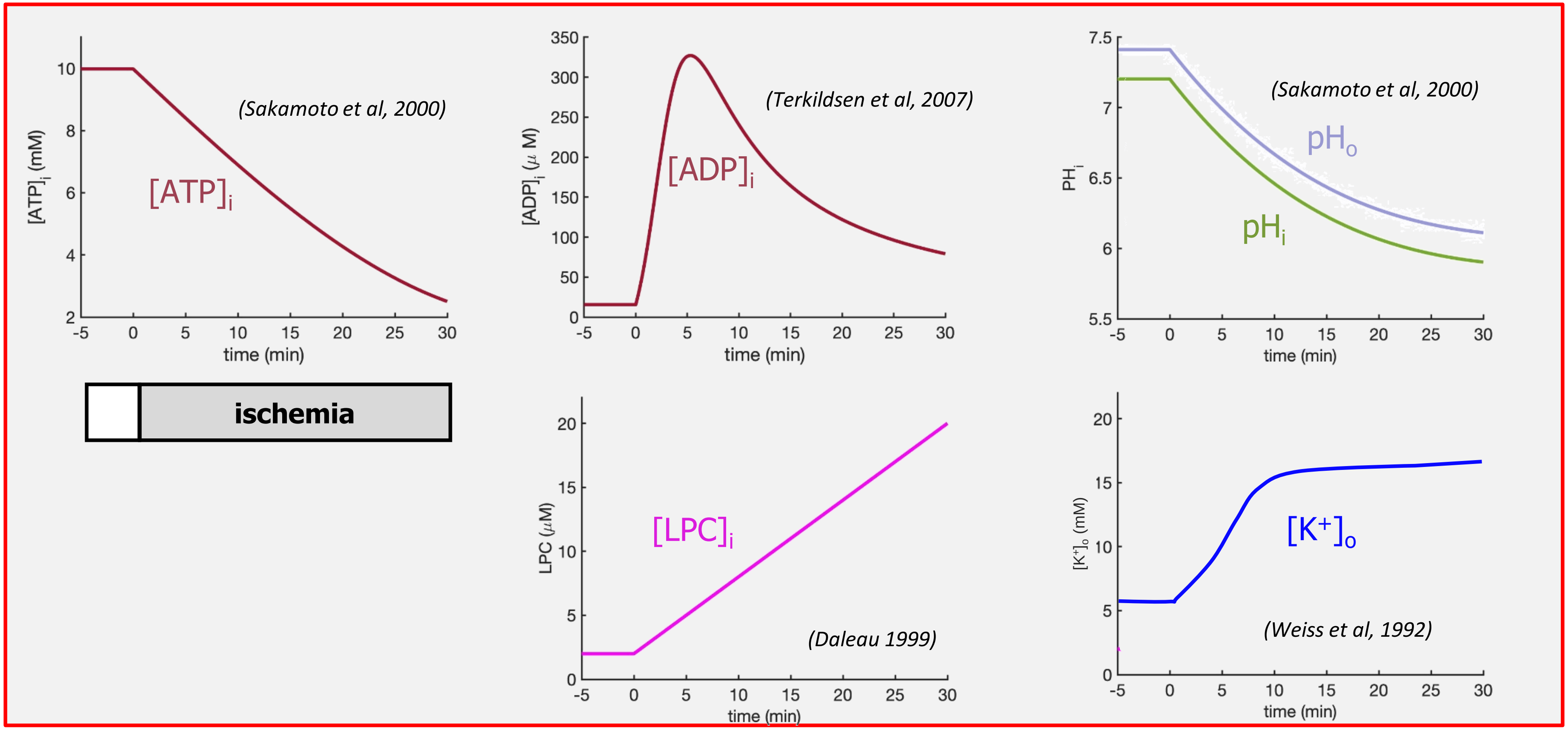
[Heidenreich et al., 2011]



[Gray et al., 1995]

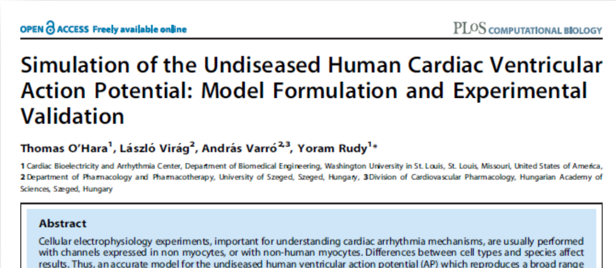
Fibrilación Ventricular

Los cambios metabólicos en isquemia miocárdica aguda…



… afectan a los canales iónicos

Modelo de potencial de acción en isquemia aguda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Simulation of the Undiseased Human Cardiac Ventricular Action Potential: Model Formulation and Experimental Validation

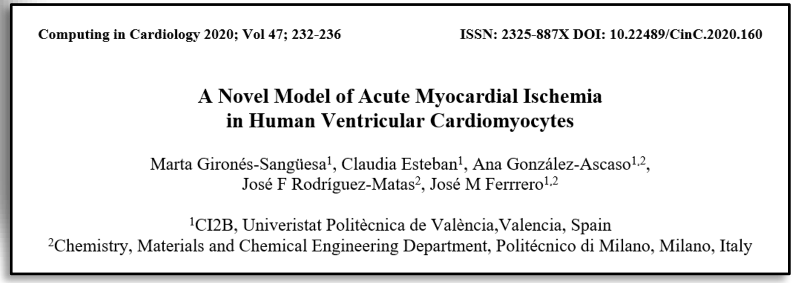
Thomas O'Hara[1], László Virág[2], András Varró[2,3], Yoram Rudy[1]*

1 Cardiac Bioelectricity and Arrhythmia Center, Department of Biomedical Engineering, Washington University in St. Louis, St. Louis, Missouri, United States of America, 2 Department of Pharmacology and Pharmacotherapy, University of Szeged, Szeged, Hungary, 3 Division of Cardiovascular Pharmacology, Hungarian Academy of Sciences, Szeged, Hungary

Abstract

Cellular electrophysiology experiments, important for understanding cardiac arrhythmia mechanisms, are usually performed with channels expressed in non myocytes, or with non-human myocytes. Differences between cell types and species affect results. Thus, an accurate model for the undiseased human ventricular action potential (AP) which reproduces a broad range

O'Hara (2011) … modificado para poder simular isquemia aguda

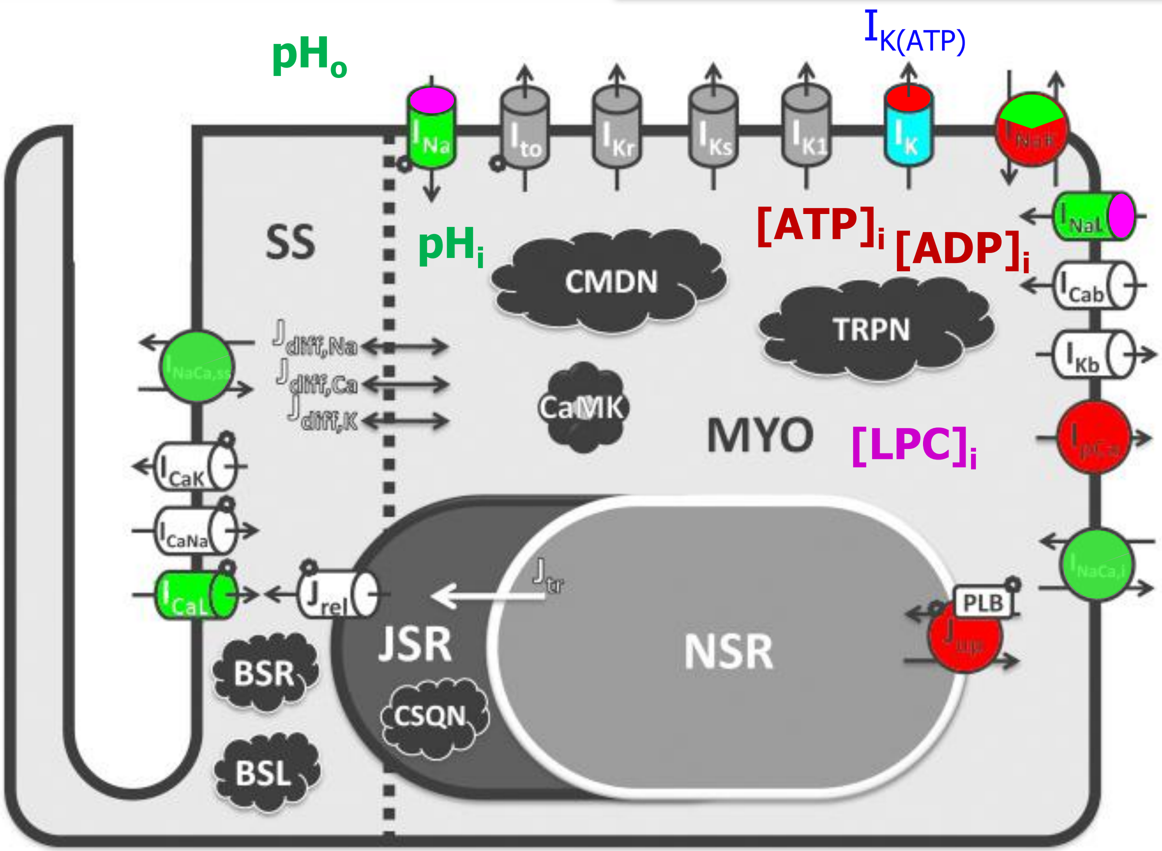

Computing in Cardiology 2020; Vol 47; 232-236 — ISSN: 2325-887X DOI: 10.22489/CinC.2020.160

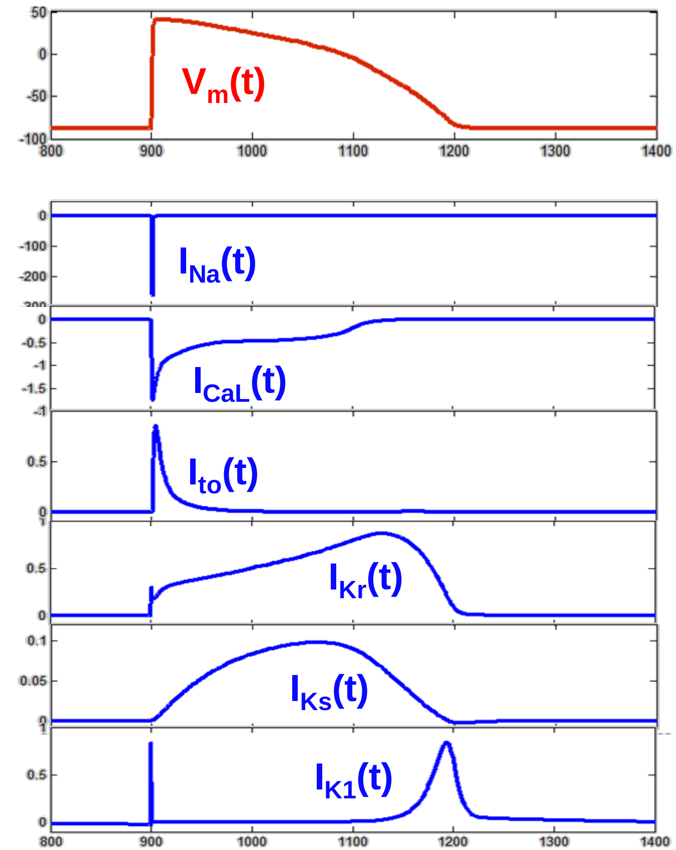
A Novel Model of Acute Myocardial Ischemia in Human Ventricular Cardiomyocytes

Marta Gironés-Sangüesa[1], Claudia Esteban[1], Ana González-Ascaso[1,2], José F Rodríguez-Matas[2], José M Ferrrero[1,2]

[1]CI2B, Univeristat Politècnica de València,Valencia, Spain
[2]Chemistry, Materials and Chemical Engineering Department, Politécnico di Milano, Milano, Italy

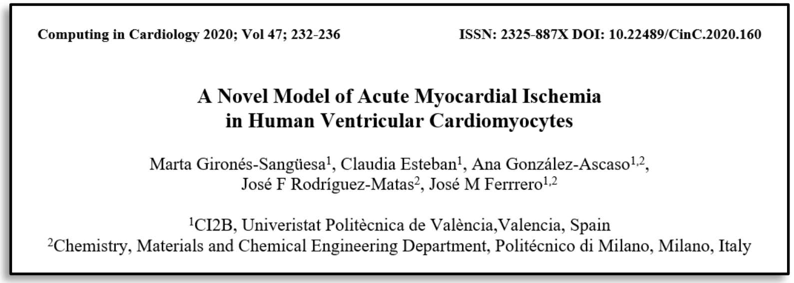
(González-Ascaso et al, 2019)
(Ferrero et al, 2003)
(Babenko et al, 1998)
(Weiss et al, 1992)
(Cortassa et al, AJP 2006)
(Ferrero et al, Circ Res 1996)





Modelo de potencial de acción en isquemia aguda

O'Hara (2011) … modificado para poder simular isquemia aguda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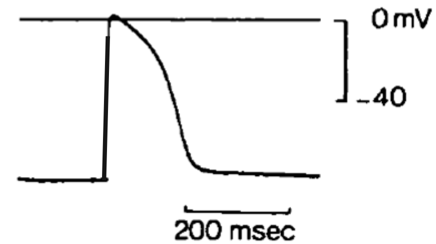
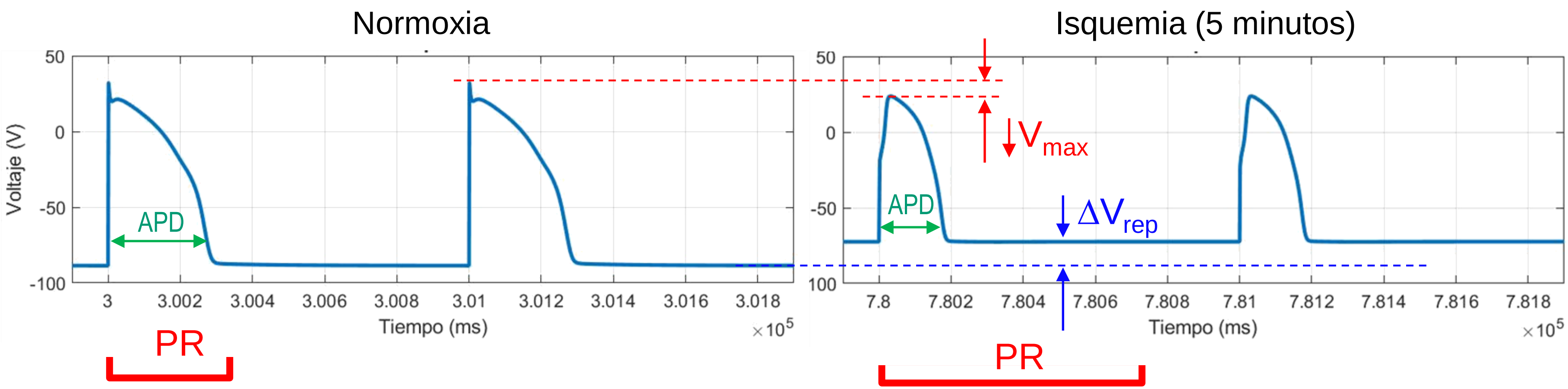
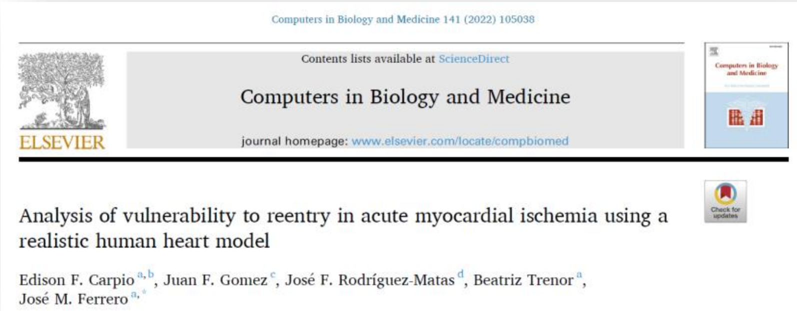




Cambios en el potencial de acción ventricular inducidos por la isquemia

- Disminución de la duración del potencial de acción (APD)
- Disminución (en valor absoluto) del potencial de reposo (V_{rep})
- Disminución de la amplitud máxima del potencial de acción (V_{max})
- Disminución de la pendiente máxima de despolarización ($\dot{V}_{max}$)
- Aumento del periodo refractario (RP)

Modelado multiescala de la isquemia miocárdica



Computers in Biology and Medicine 141 (2022) 105038

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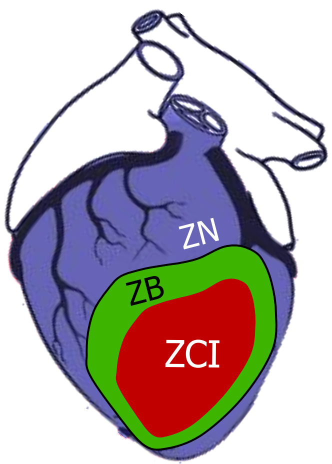
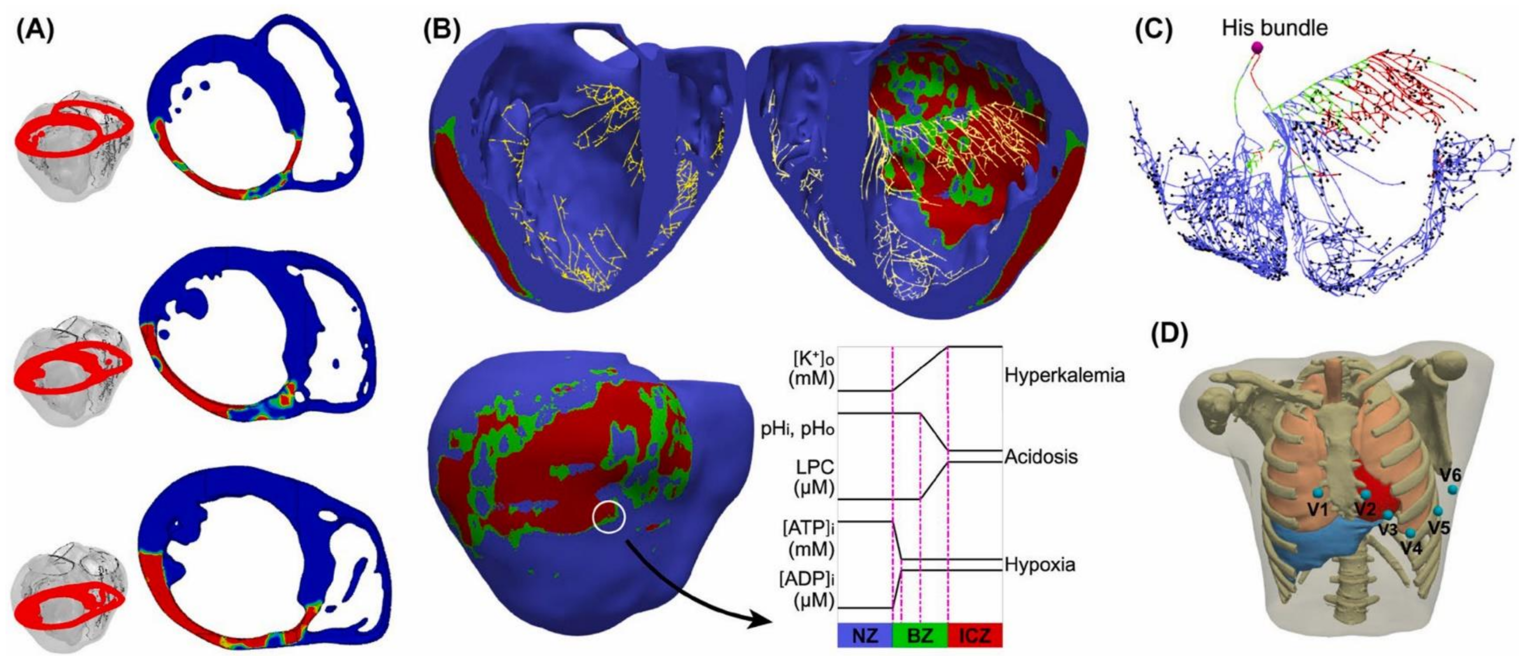
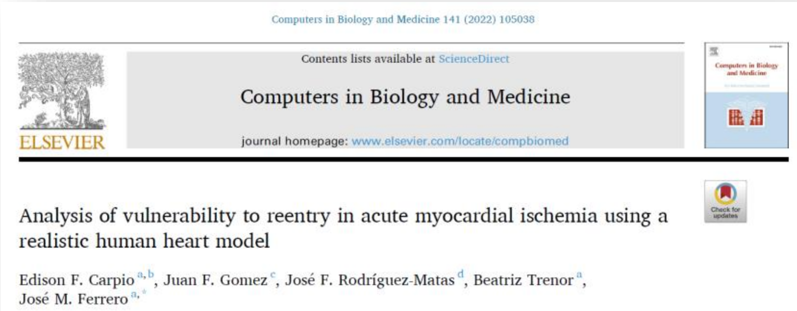




[Carpio *et al.*, 2020]

Modelado multiescala de la isquemia miocárdica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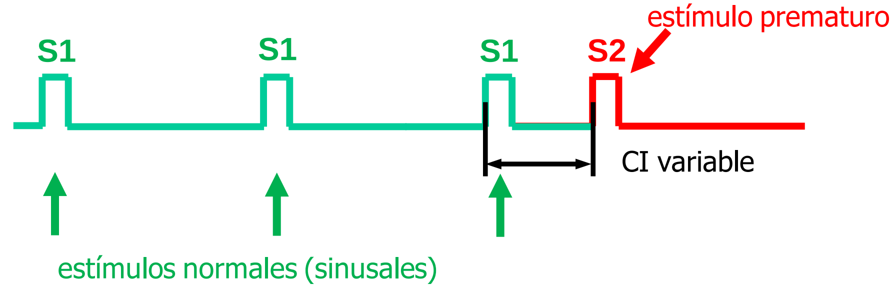

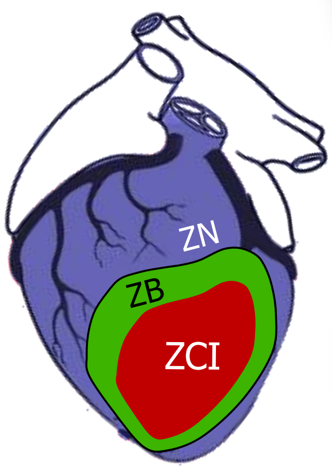

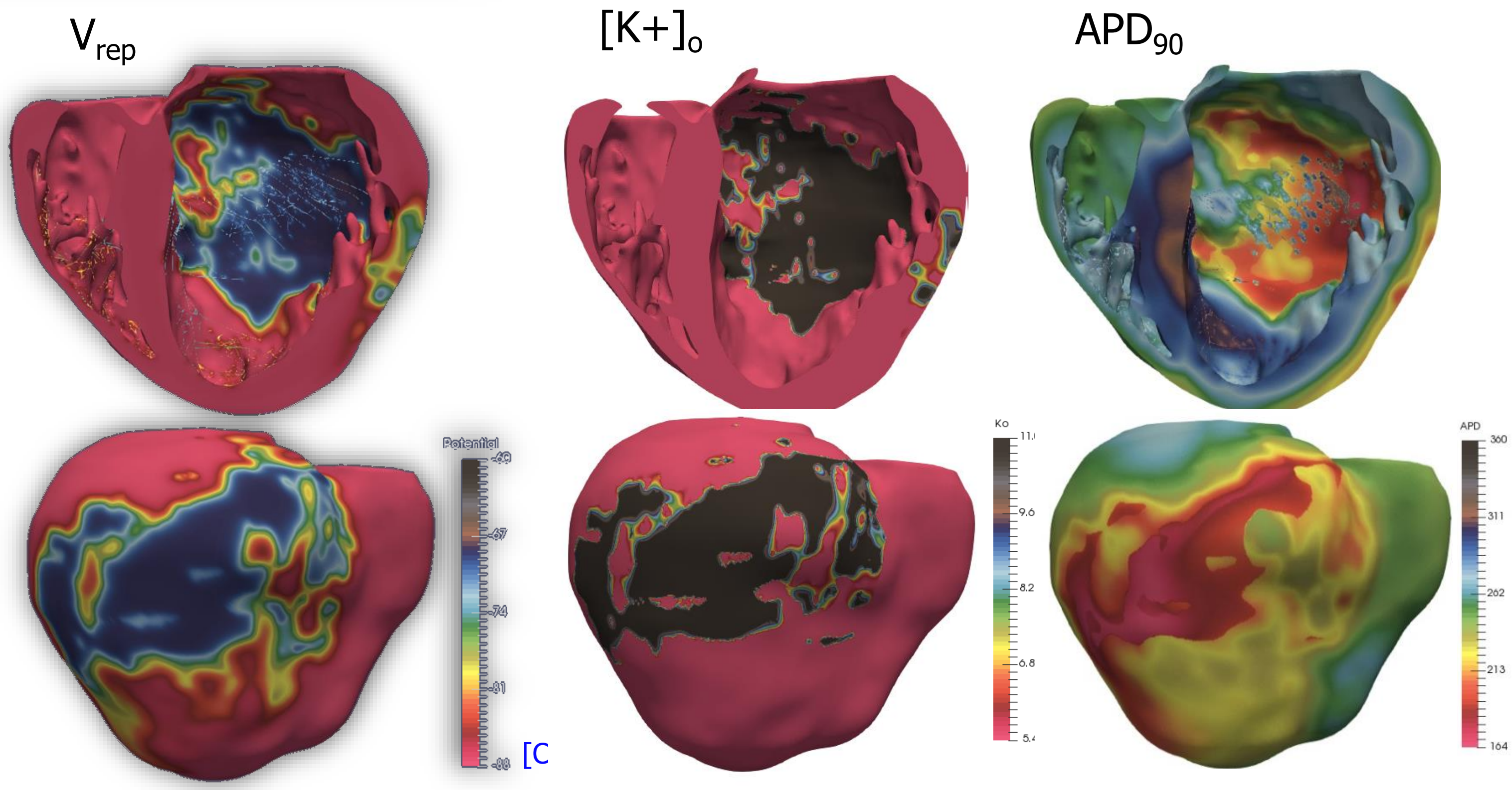

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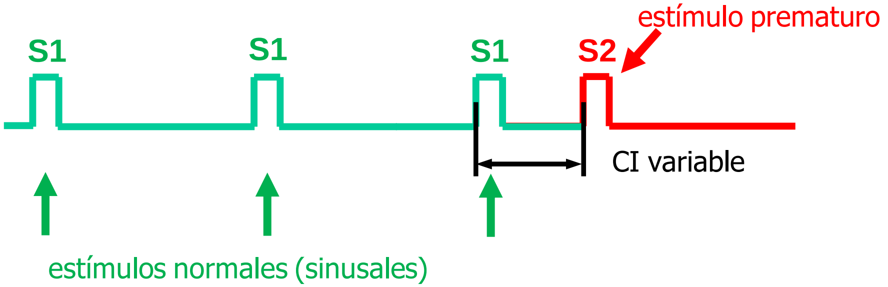
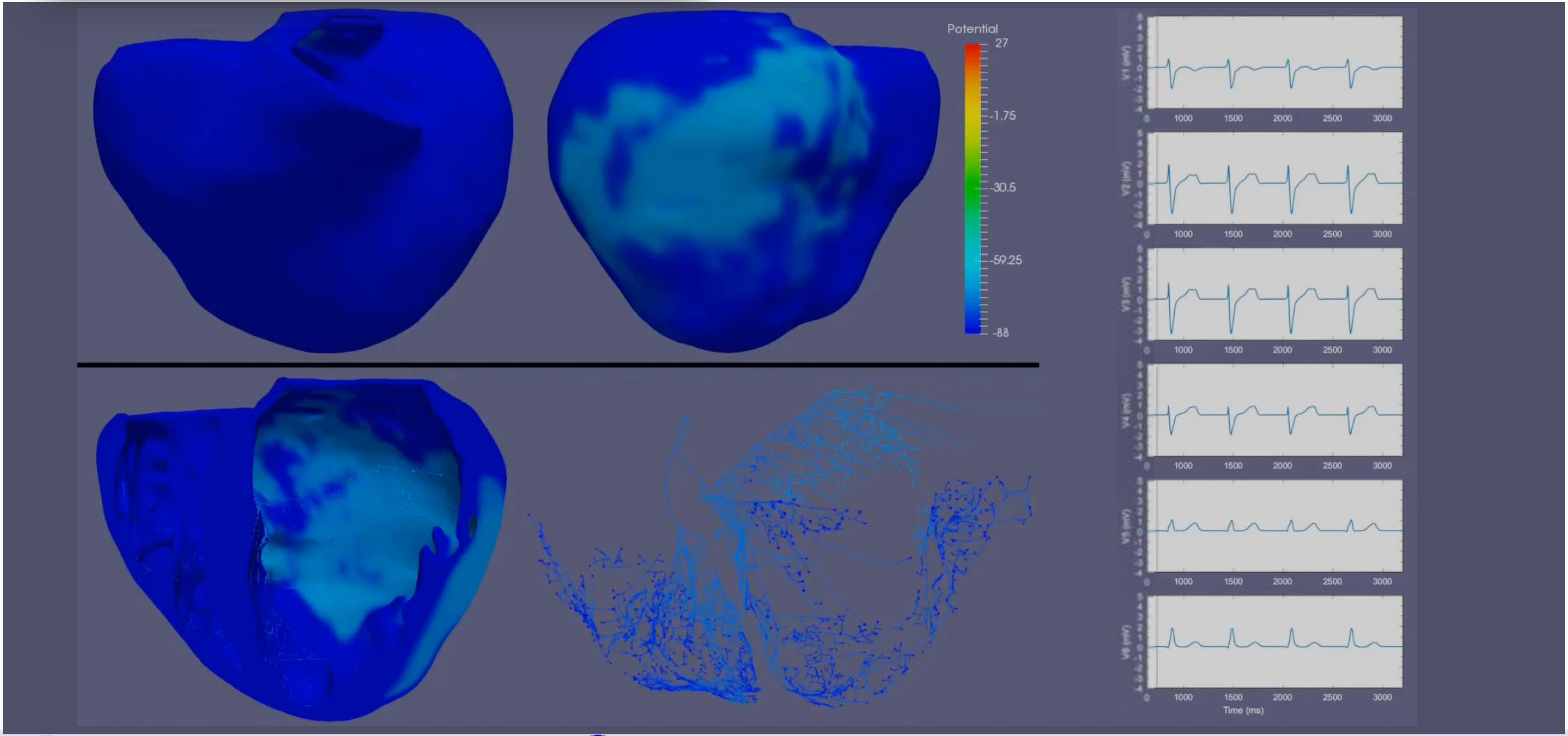
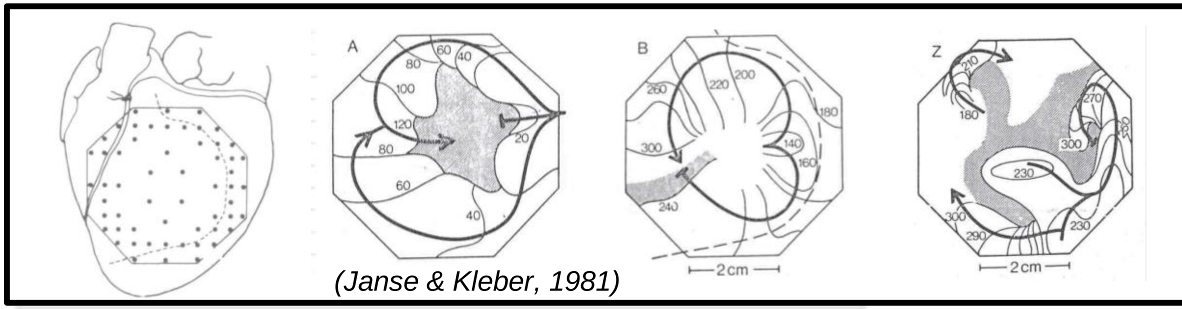
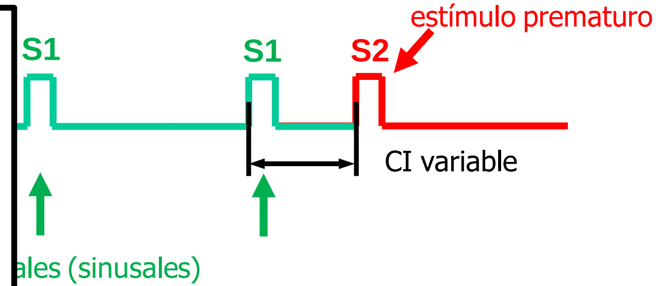


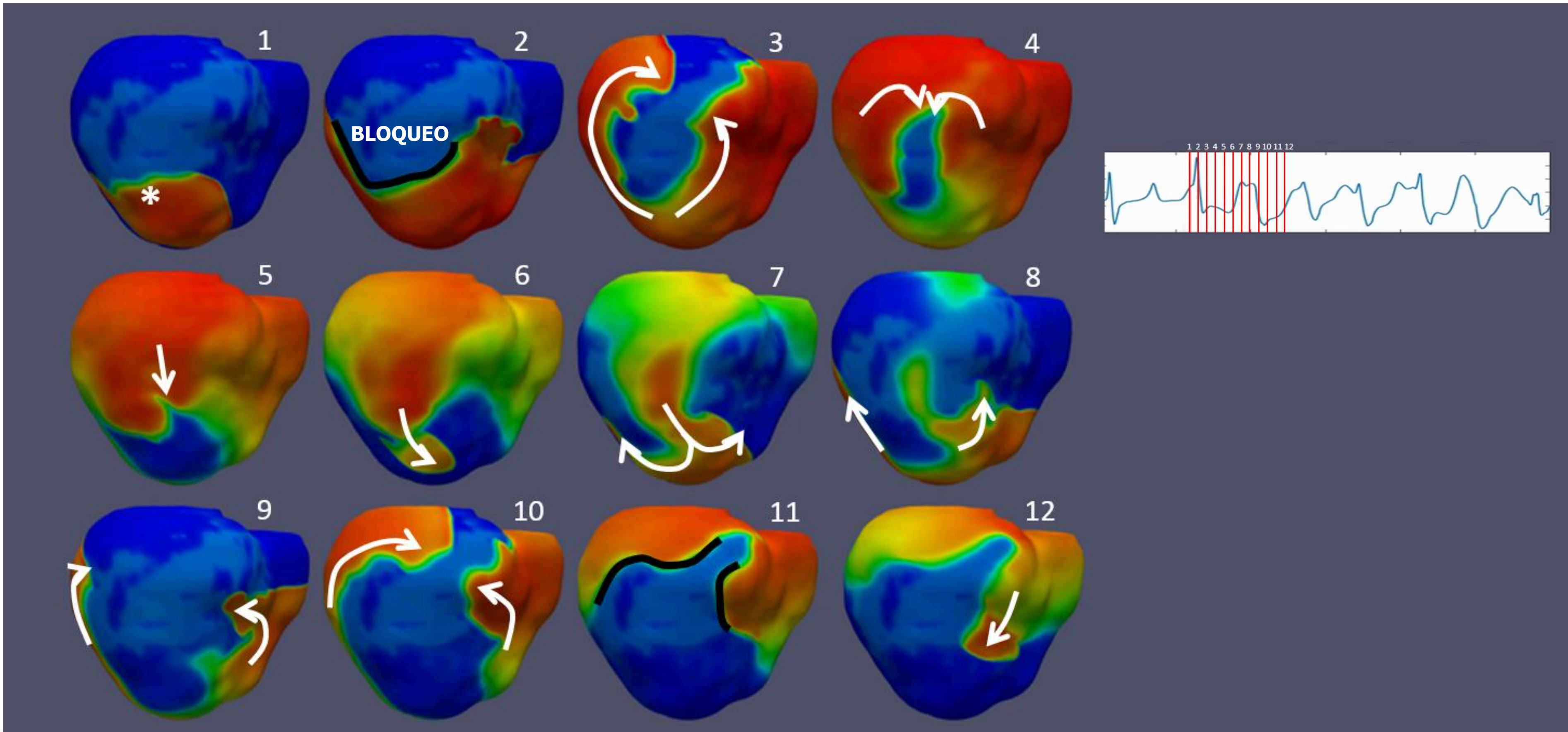


Modelado multiescala de la isquemia miocárdica



(Janse & Kleber, 1981)





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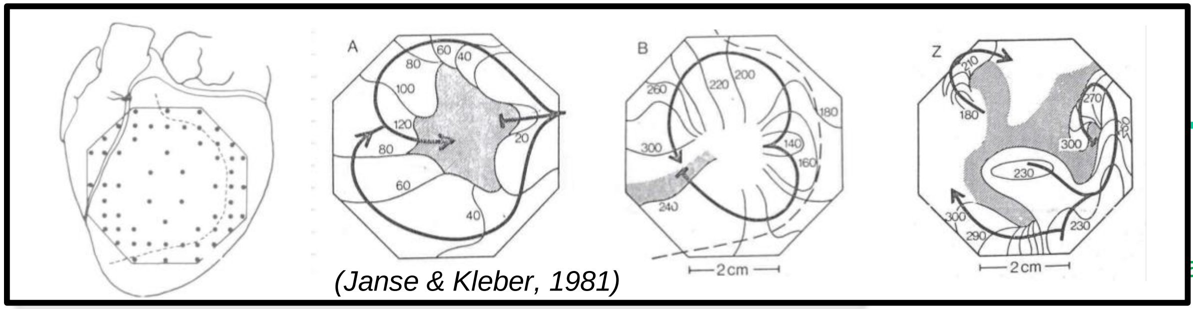

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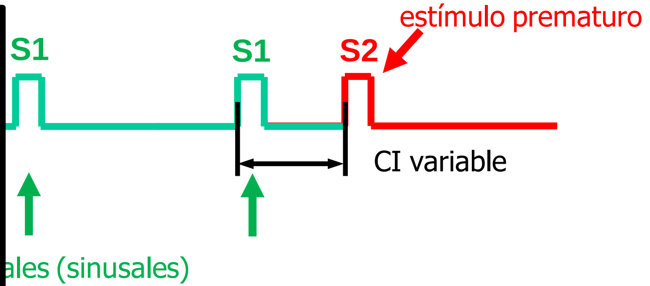

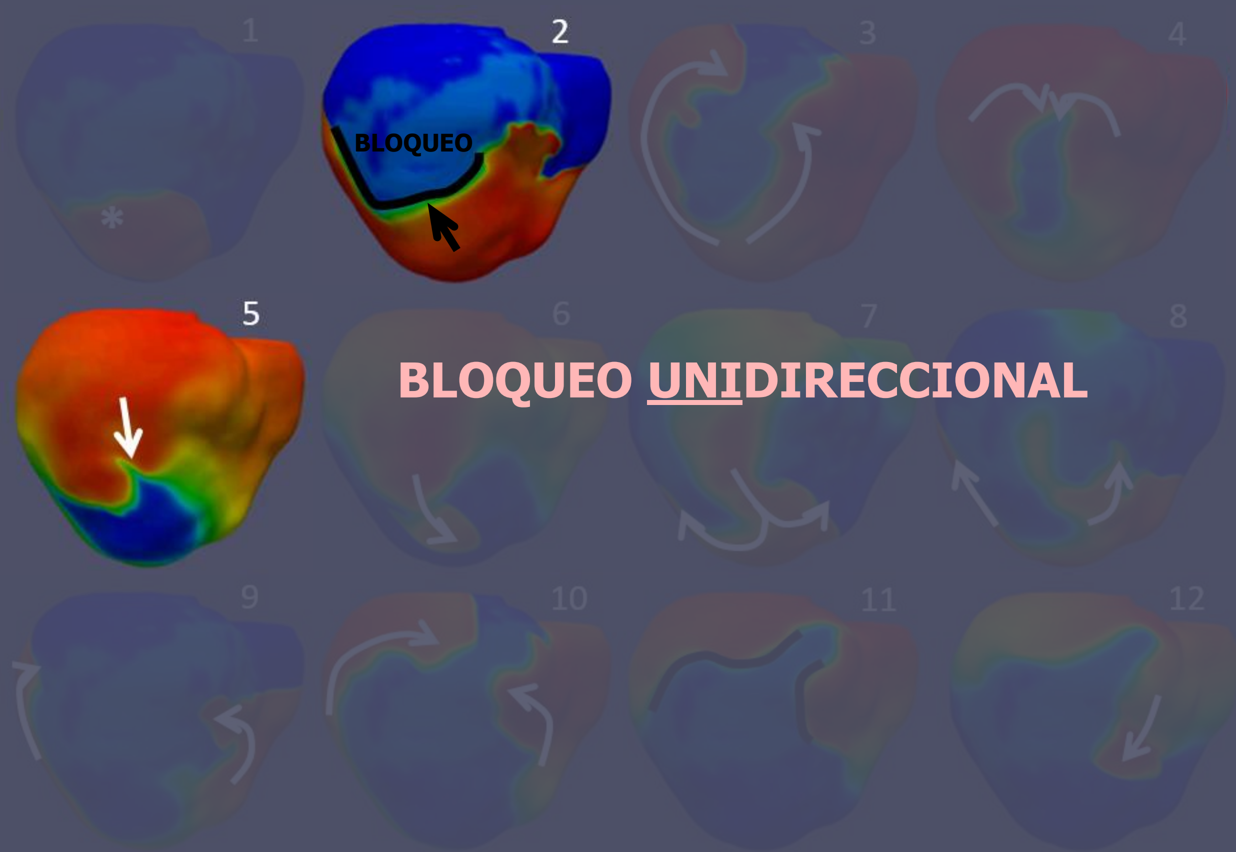

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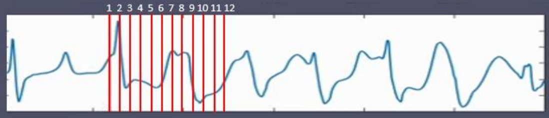
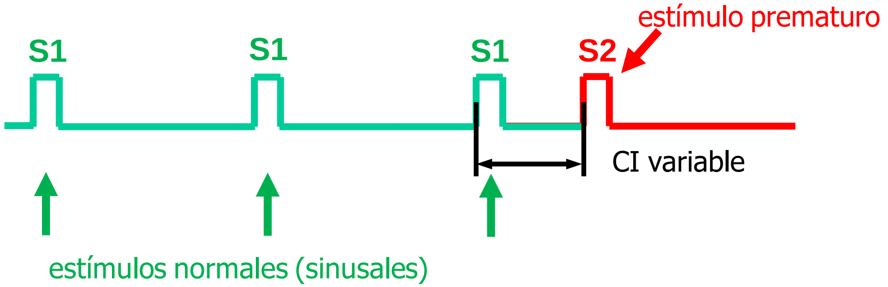
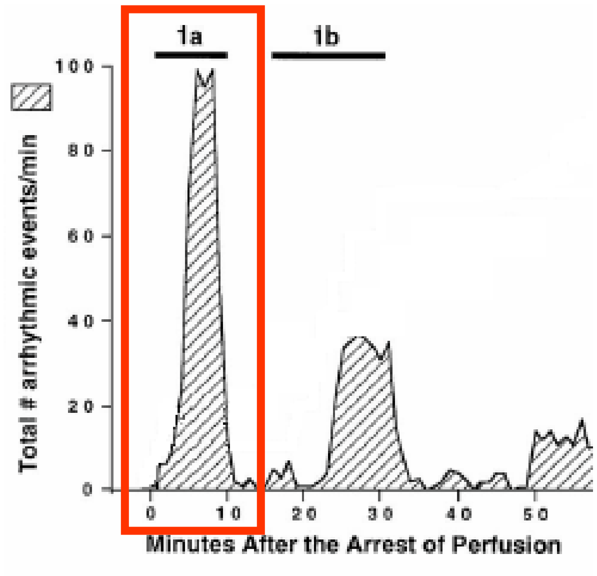
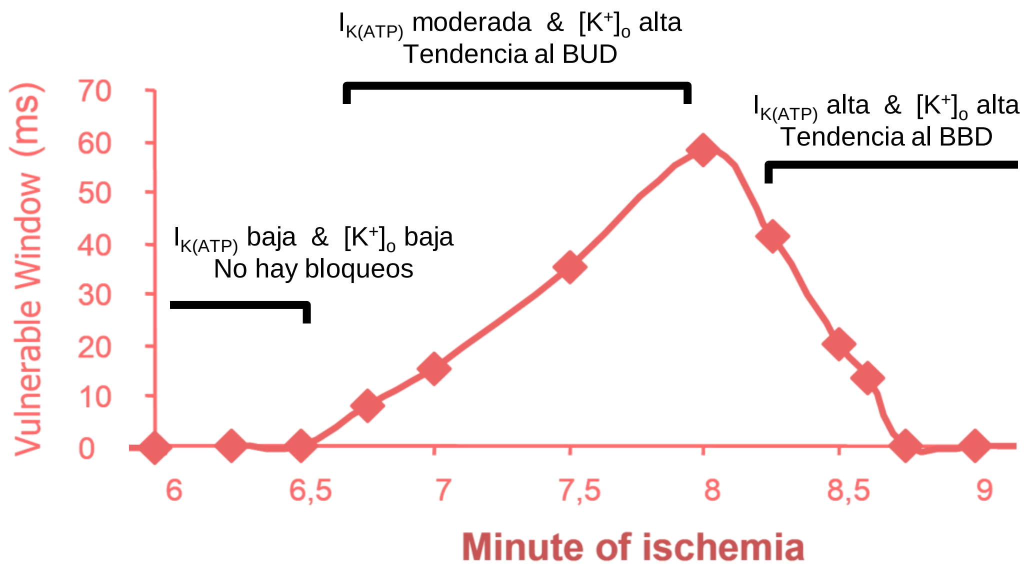


Vulnerabilidad a las arritmias en isquemia miocárdica

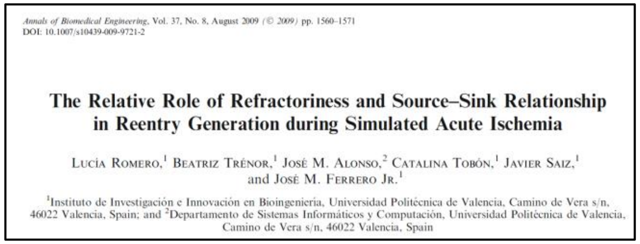




adapted from Smith *et al*. Circulation 92:3051– 60, 1995



Romero *et al*.,Ann Biomed Eng 2009



Annals of Biomedical Engineering, Vol. 37, No. 8, August 2009 (© 2009) pp. 1560–1571
DOI: 10.1007/s10439-009-9721-2

The Relative Role of Refractoriness and Source–Sink Relationship in Reentry Generation during Simulated Acute Ischemia

Lucía Romero,[1] Beatriz Trénor,[1] José M. Alonso,[2] Catalina Tobón,[1] Javier Saiz,[1] and José M. Ferrero Jr.[1]

[1]Instituto de Investigación e Innovación en Bioingeniería, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain; and [2]Departamento de Sistemas Informáticos y Computación, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain

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9.1.- Fundamentos bioeléctricos de las arritmias por reentrada

9.2.- Simulación computacional de arritmias en isquemia miocárdica aguda

9.3.- Efecto de fármacos en arritmias en isquemia miocárdica aguda

9.4.- Terapia de ablación en infarto crónico

9.5.- Construcción de un modelo cardiaco 3D personalizado a paciente

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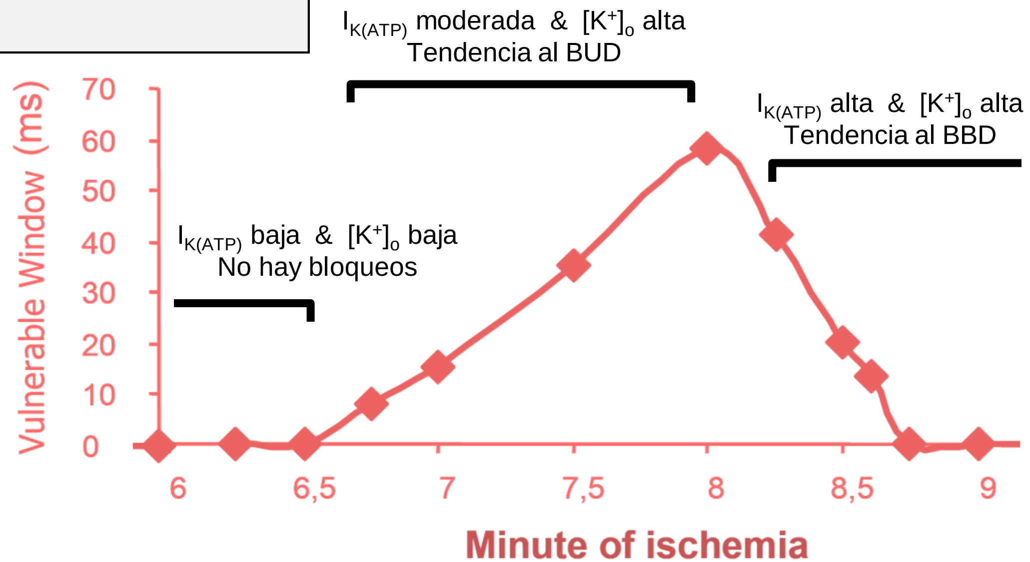

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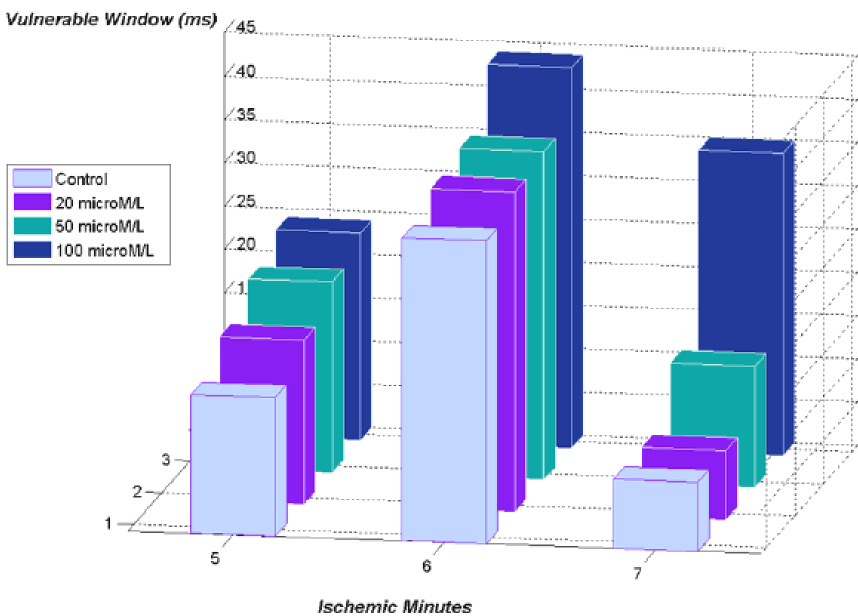
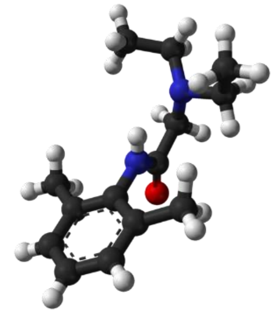
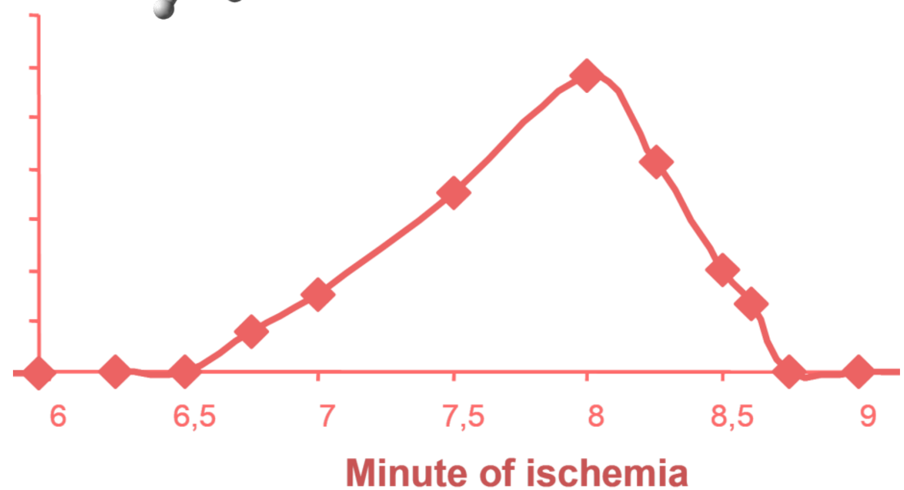
Efecto de fármacos en isquemia aguda

La lidocaína modula la vulnerabilidad a la FV en isquemia aguda







Cardona *et al*., Am J Physiol 2010

Am J Physiol Heart Circ Physiol 299: H1615–H1624, 2010.
First published August 13, 2010; doi:10.1152/ajpheart.00425.2010.

Exploring the role of pH in modulating the effects of lidocaine in virtual ischemic tissue

Karen Cardona,[1] Beatriz Trénor,[1] Germán Moltó,[2] Miguel Martínez,[3] José María Ferrero, Jr.,[1] Frank Starmer,[4] and Javier Saiz[1]

[1]Instituto de Investigación Interuniversitario en Bioingeniería y Tecnología Orientada al Ser Humano, [2]Departamento de Sistemas Informáticos y Computación, and [3]Instituto Universitario de Automática e Informática Industrial, Universidad Politécnica de Valencia, Valencia, Spain; and [4]Biostatistics and Bioinformatics, Duke University, Singapore

Submitted 3 May 2010; accepted in final form 10 August 2010

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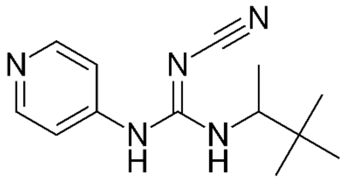
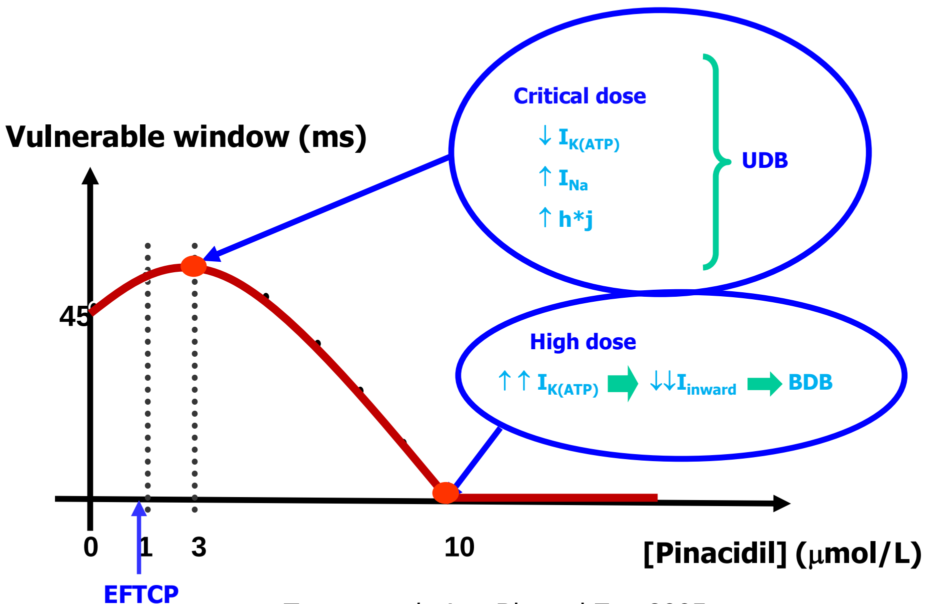
Efecto de fármacos en isquemia aguda

El pinacidil modula la vulnerabiliad a la FV en isquemia aguda





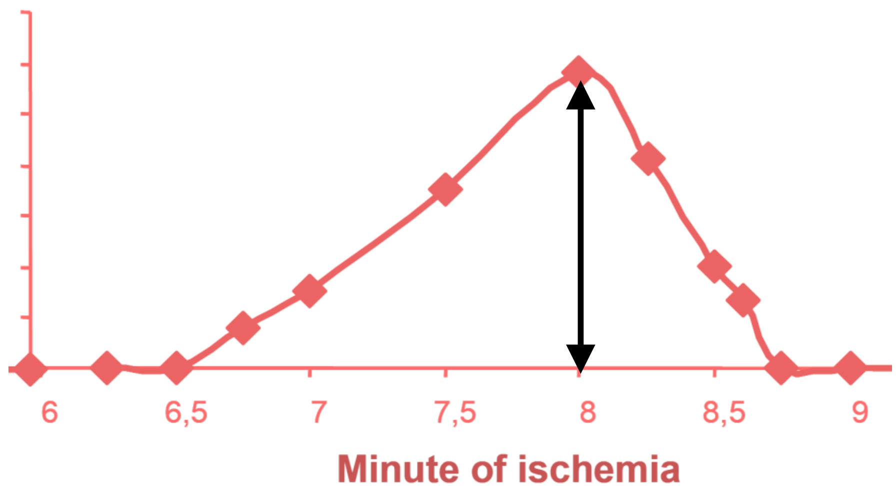
Trenor *et al*., Ann Biomed Eng 2005

Annals of Biomedical Engineering, Vol. 33, No. 7, July 2005 (© 2005) pp. 897–906
DOI: 10.1007/s10439-005-3554-4

Effects of Pinacidil on Reentrant Arrhythmias Generated During Acute Regional Ischemia: A Simulation Study

Beatriz Trénor,[1] José M. Ferrero, Jr.,[1] Blanca Rodríguez,[2] and Fulgencio Montilla[1]

[1]Centro de Investigación e Innovación en Bioingeniería, Departamento de Ingeniería Electrónica, Universidad Politécnica de Valencia, Camino de Vera s/n, 46022 Valencia, Spain and [2]Oxford University Computing Laboratory, Wolfson Building, Parks Road, Oxford OX1 3QD, UK



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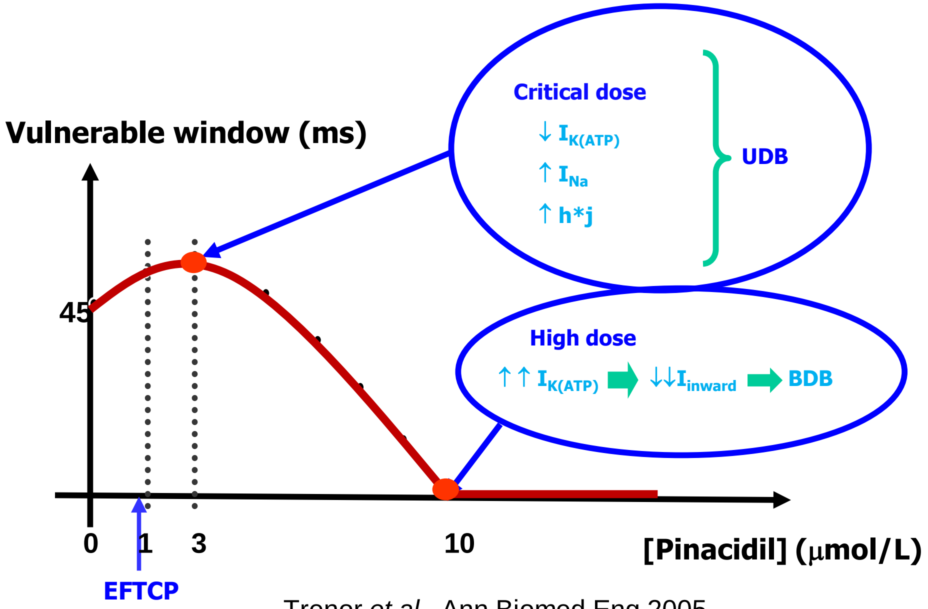

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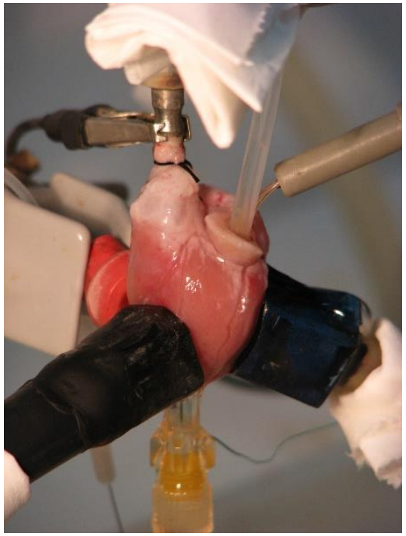

A Ferrero et al, 2005

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CRÉDITOS…

Universidad Nacional de Lomas de Zamora, Argentina

Elvio Heidenreich

Hospital Clínico Universitario de Valencia

Maite Izquierdo
Ricardo Ruiz

Hospital Clínic Universitari de València

Universidad Politécnica de Valencia, España

Chema Ferrero
Alejandro López
Dani Ferrero

UNIVERSITAT POLITÈCNICA DE VALÈNCIA

Universidad Internacional de Valencia, España

Juan Francisco Gómez

viu Universidad Internacional de Valencia

Universidad de Valencia, España

Rafa Sebastián

VNIVERSITAT DE VALÈNCIA

King's College, London, UK

Martin Bishop

KING'S COLLEGE

Politécnico di Milano, Italia

José Félix Rodríguez

POLITECNICO MILANO 1863

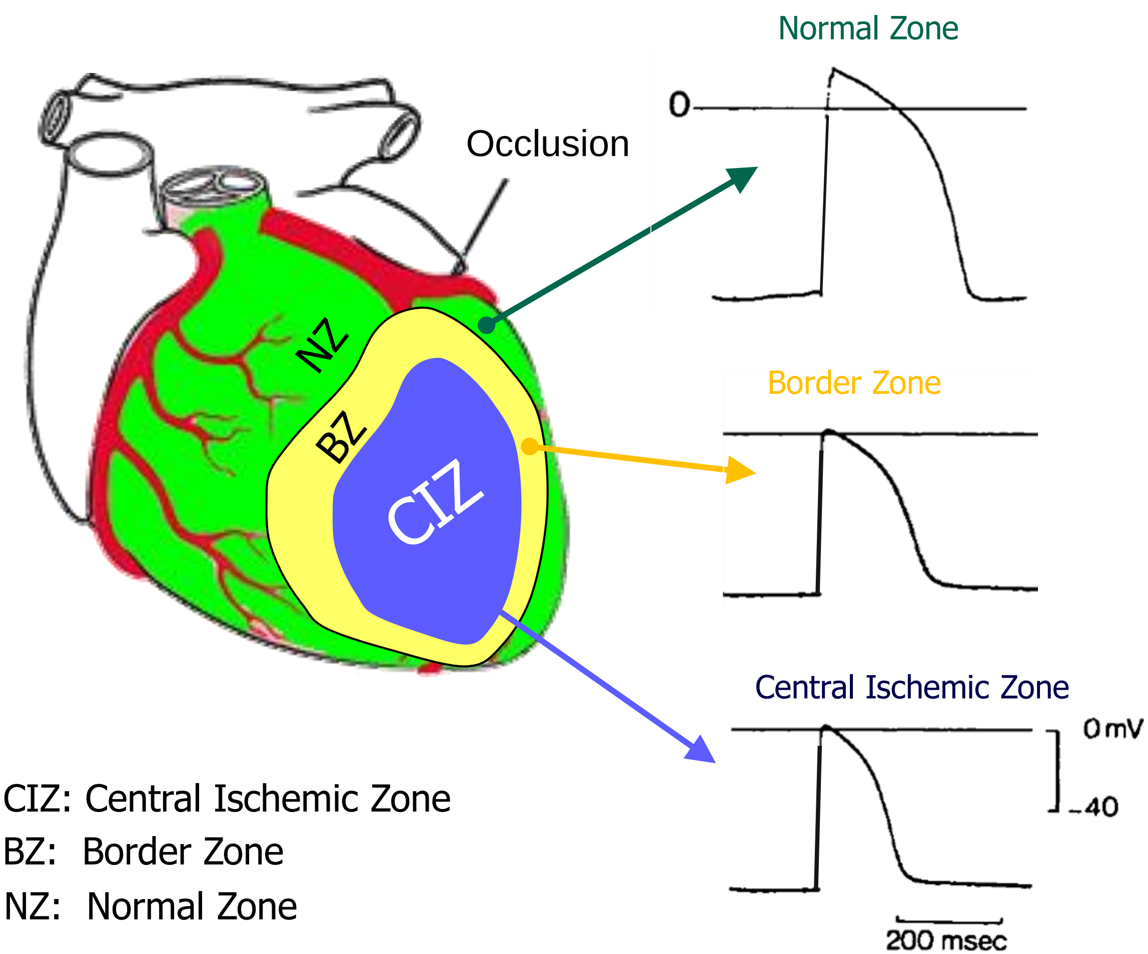
Universidad de Zaragoza, España

Andrés Mena-Tóbar

1542 Universidad Zaragoza

Myocardial ischemia and infarction

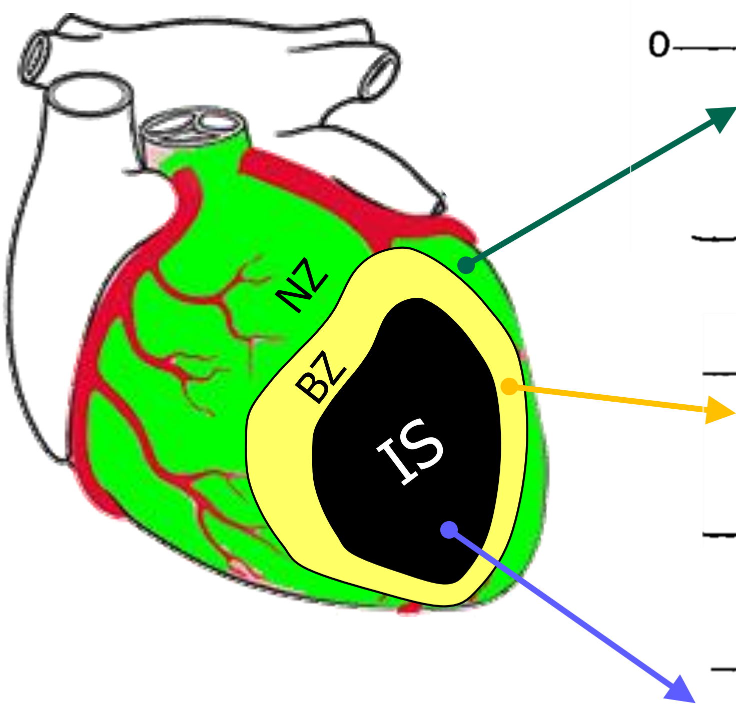
0-30 min: ACUTE ISCHEMIA

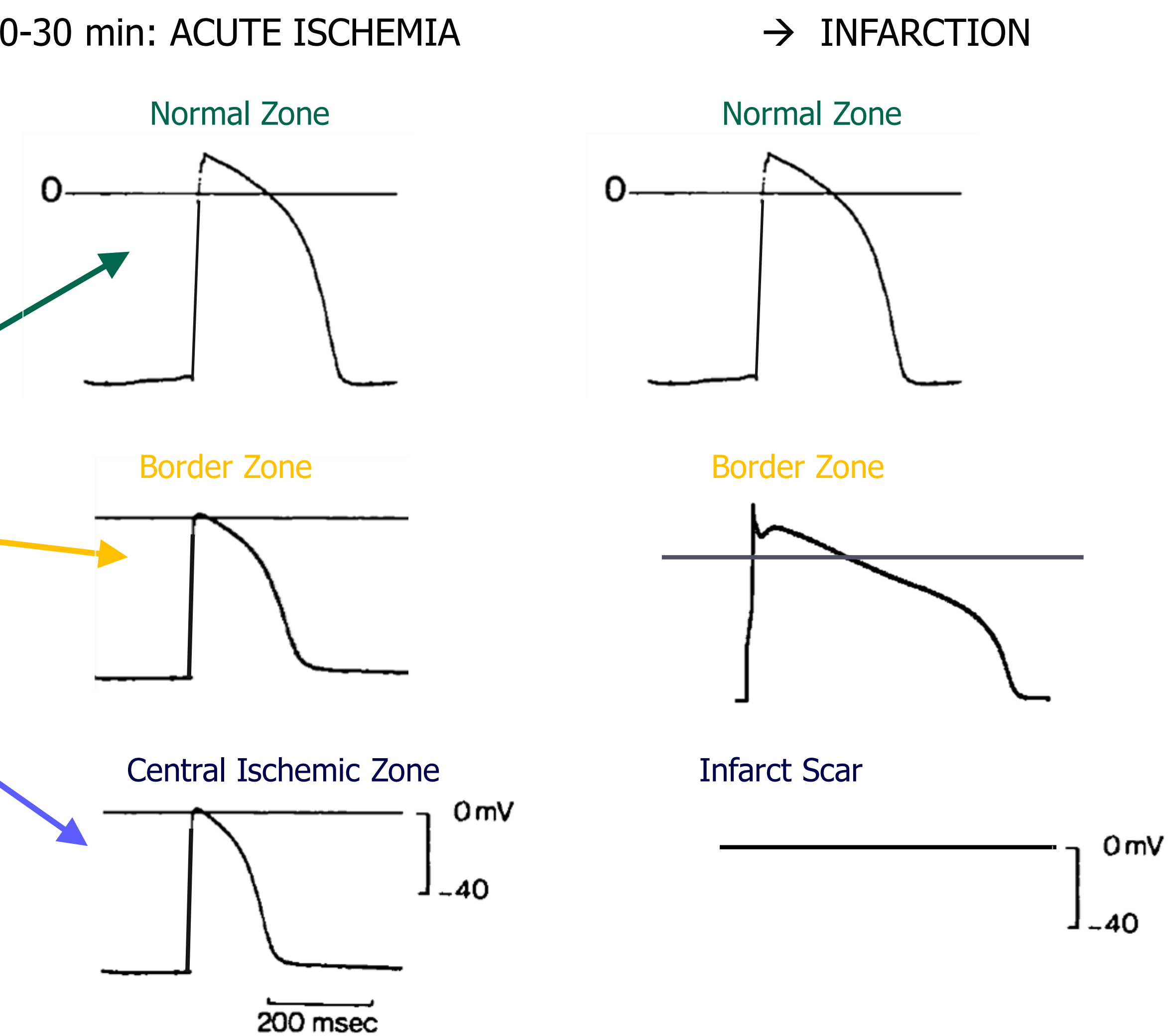


Hours later…

CIZ: Central Ischemic Zone
BZ: Border Zone
NZ: Normal Zone

Myocardial ischemia and infarction



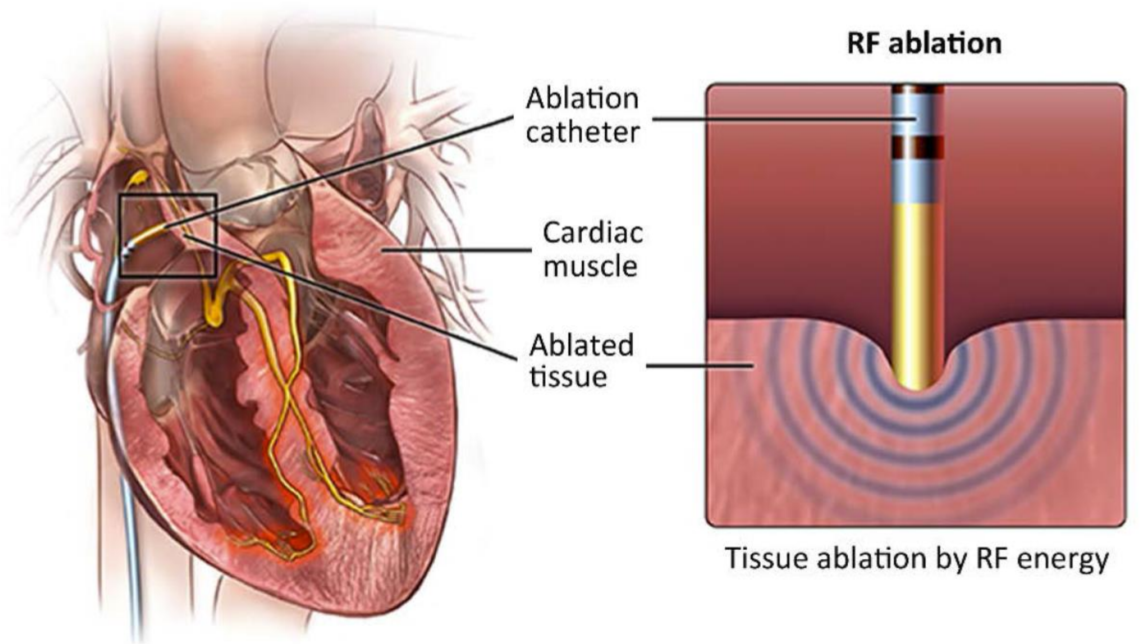


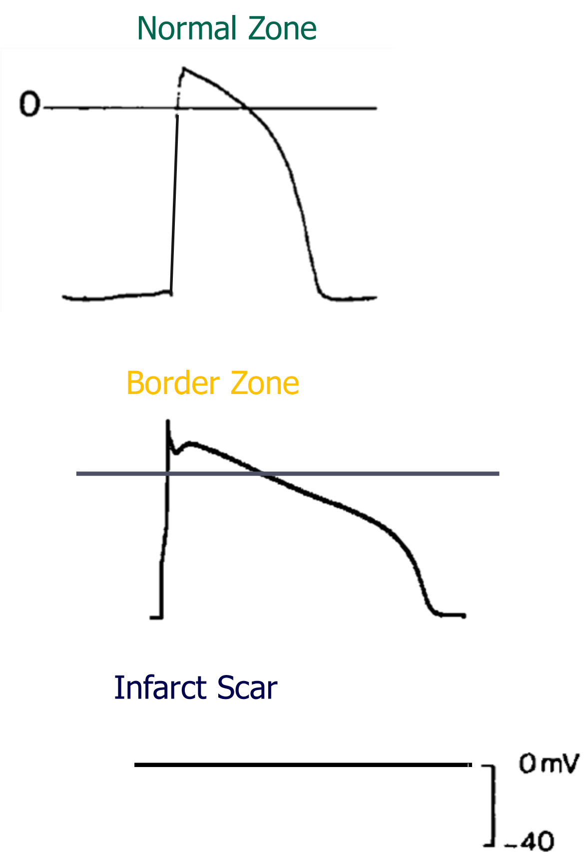
IS: Infarct Scar (NON excitable)
BZ: Border Zone
NZ: Normal Zone

Myocardial ischemia and infarction

Months/years after the infarction…

INFARCTION



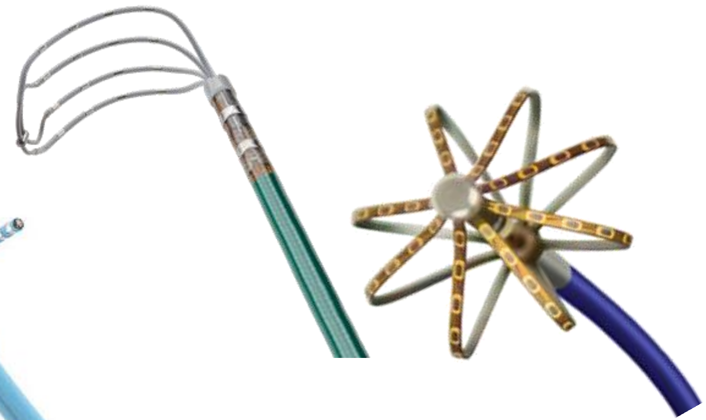


IS: Infarct Scar (NON excitable)

BZ: Border Zone

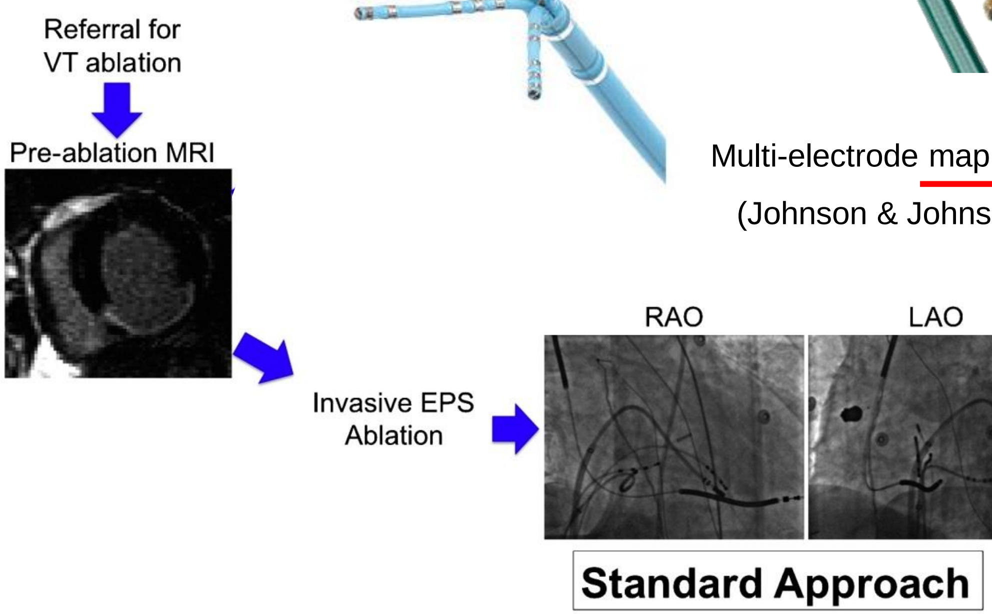
NZ: Normal Zone

Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia



Multi-electrode mapping and ablation catheters

(Johnson & Johnson, St. Jude, Boston Sc.)

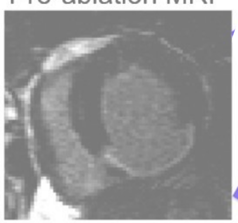


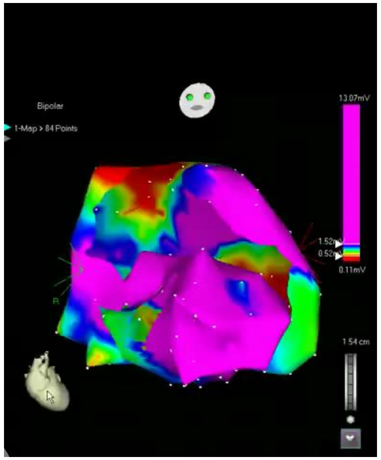
[adapted from Ashikaga et al, *Heart Rhythm* 2013]

Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

Referral for VT ablation

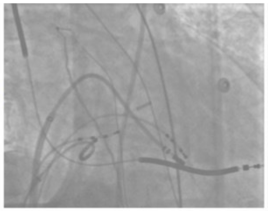
Pre-ablation MRI



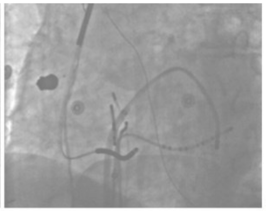


Invasive EPS Ablation

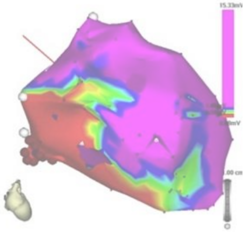
RAO



LAO



CARTO



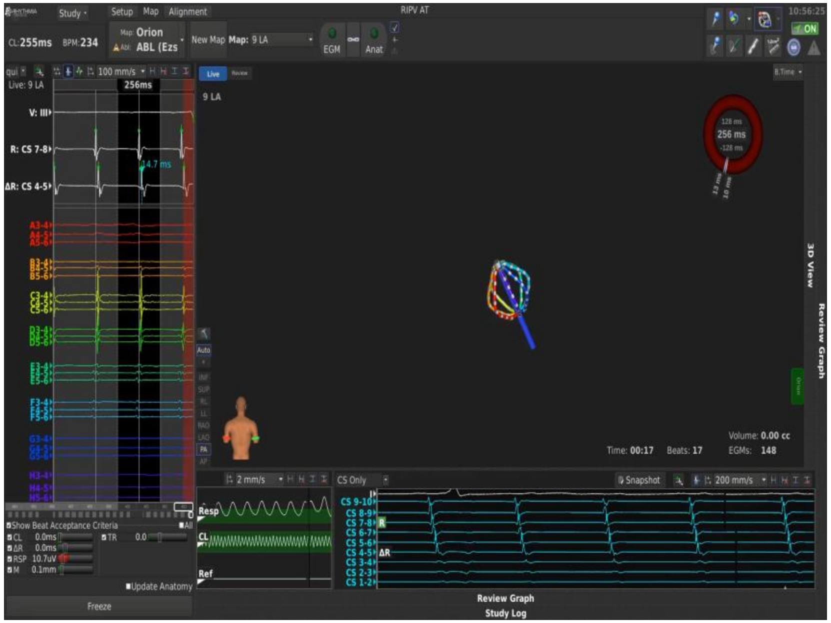
Standard Approach

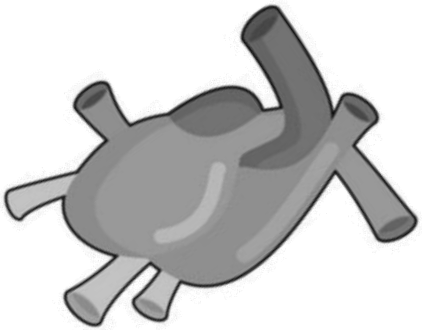
[adapted from Ashikaga et al, *Heart Rhythm* 2013]

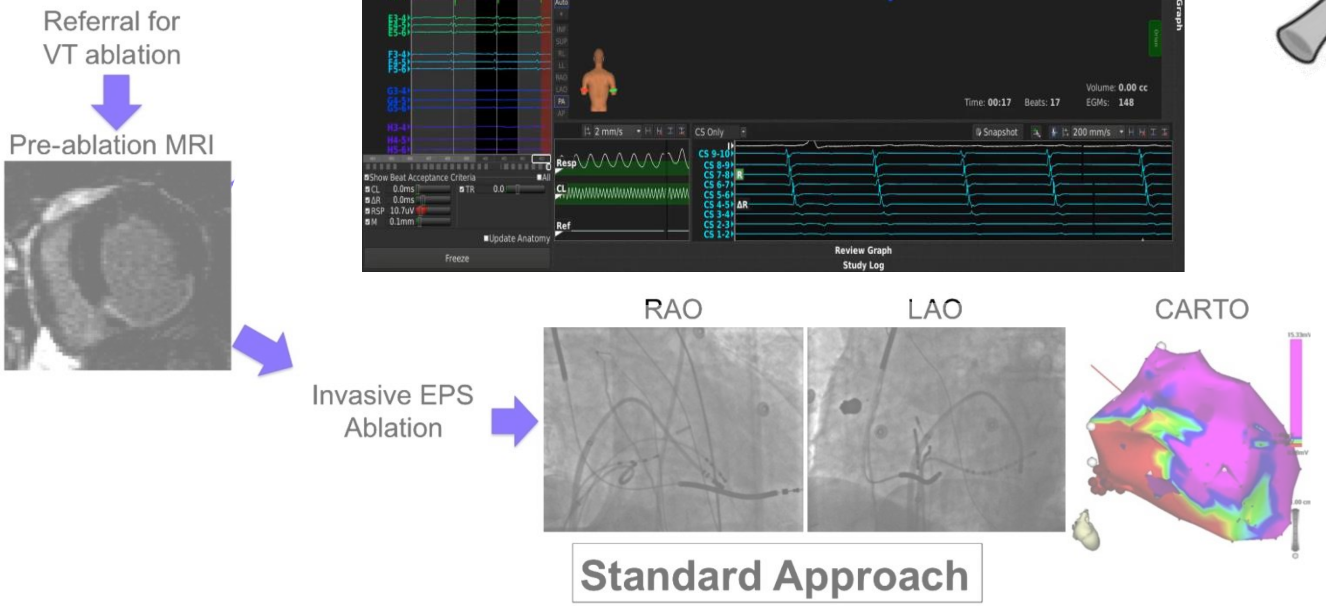
Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

INTELLA MIFI (Boston Sci.)

Real time: 16 minutes



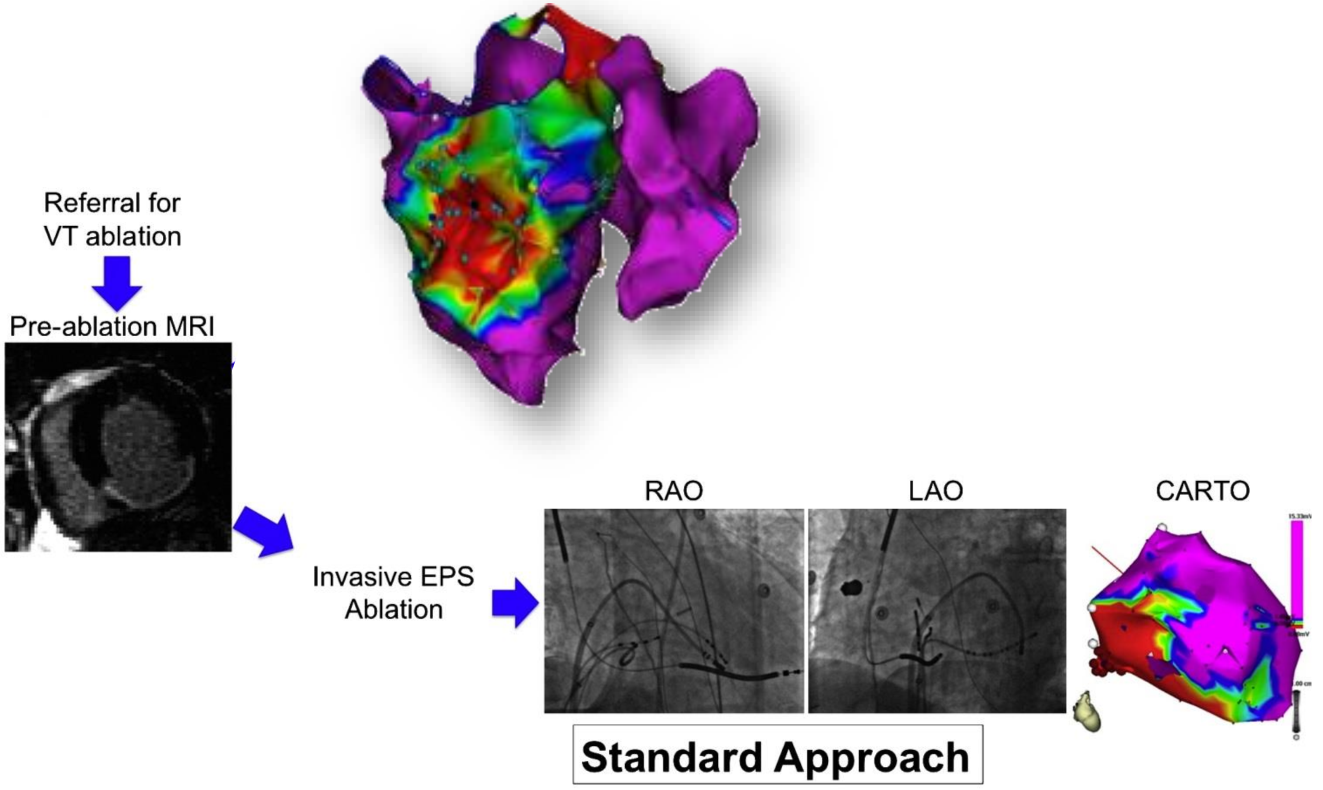




[adapted from Ashikaga et al, *Heart Rhythm* 2013]

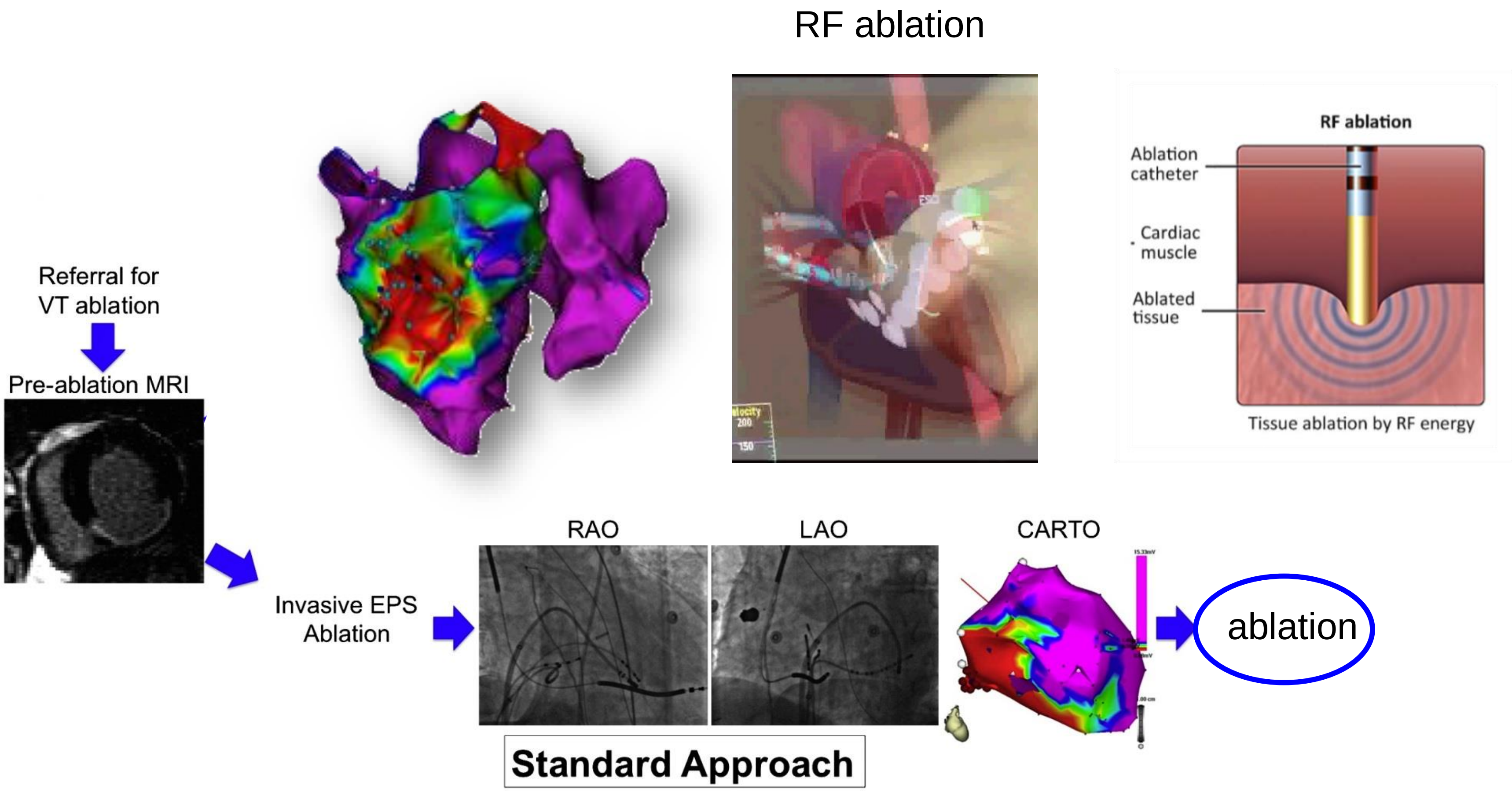
Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

Electroanatomical map of the endocardium…



[adapted from Ashikaga et al, *Heart Rhythm* 2013]

Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia



[adapted from Ashikaga et al, *Heart Rhythm* 2013]

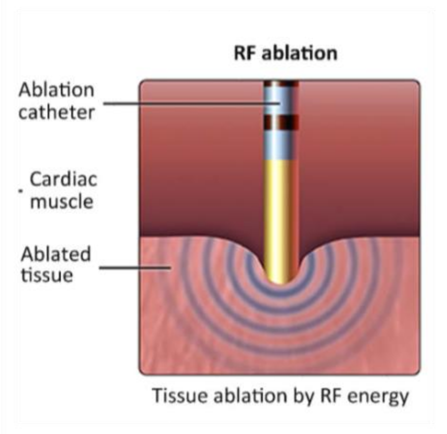
Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

Personalized Cardiac Computational Models: From Clinical Data to Simulation of Infarct-Related Ventricular Tachycardia

frontiers in Physiology

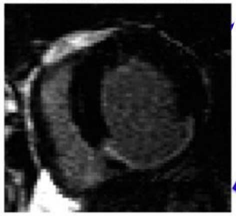
Alejandro Lopez-Perez[1], Rafael Sebastian[2], M. Izquierdo[3,4], Ricardo Ruiz[3,4], Martin Bishop[5] and Jose M. Ferrero[1]*

In the chronic stage of myocardial infarction, a significant number of patients develop life-threatening ventricular tachycardias (VT) due to the arrhythmogenic nature of the remodeled myocardium. Radiofrequency ablation (RFA) is a common procedure to isolate reentry pathways across the infarct scar that are responsible for VT. Unfortunately, this strategy show relatively low success rates; up to 50% of patients experience recurrent VT after the procedure. In the last decade, intensive research in the field of computational cardiac electrophysiology (EP) has demonstrated the

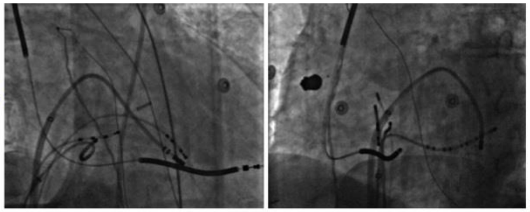


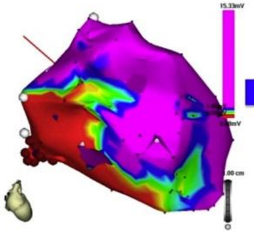
Referral for VT ablation

Pre-ablation MRI



Invasive EPS Ablation



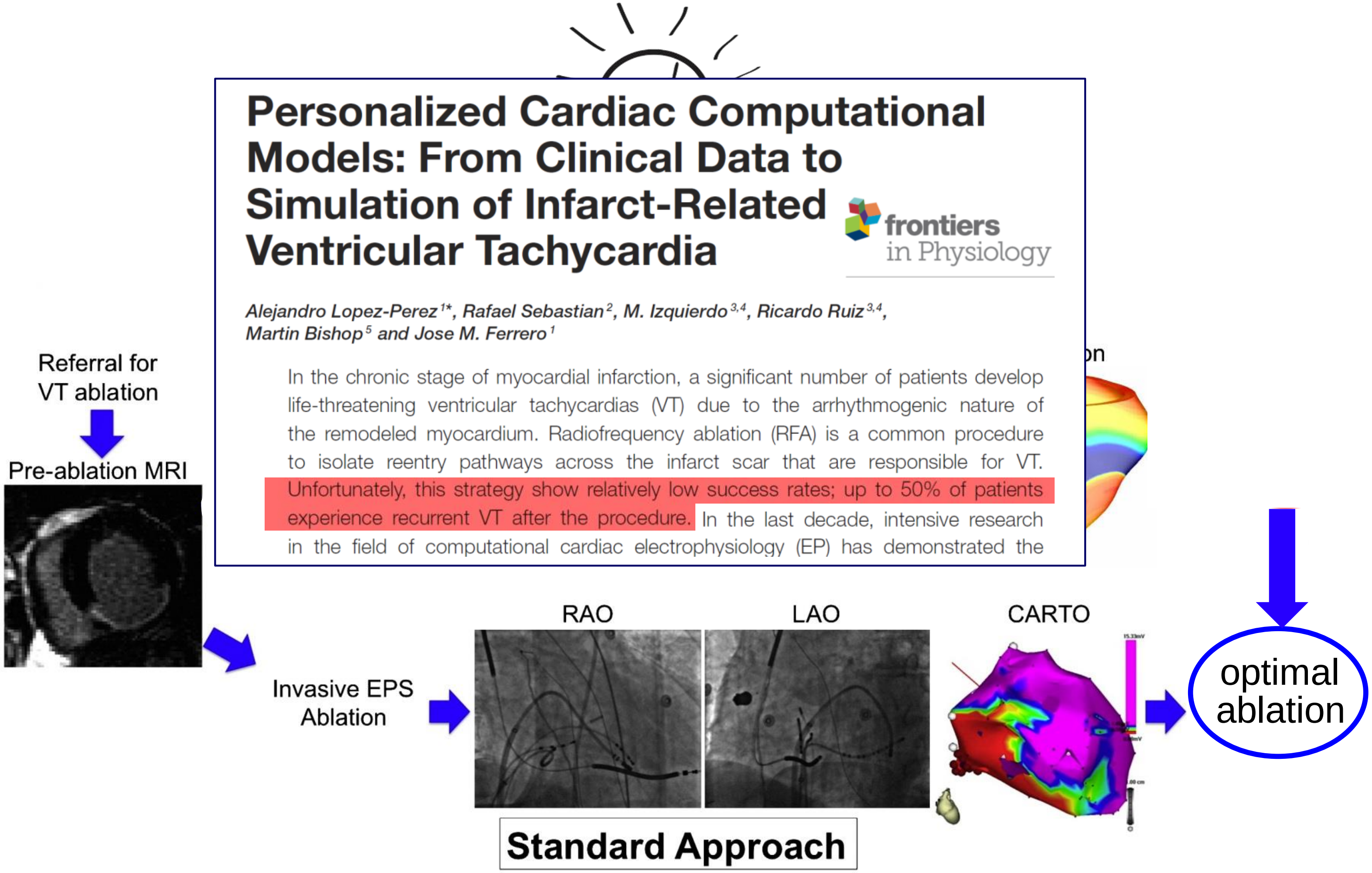


ablation

Standard Approach

[adapted from Ashikaga et al, *Heart Rhythm* 2013]

Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia



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frontiers in Physiology

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[adapted from Ashikaga et al, *Heart Rhythm* 2013]

… the computational model must be personalized (i.e. patient-specific)

Tema 9

9.1.- Fundamentos bioeléctricos de las arritmias por reentrada

9.2.- Simulación computacional de arritmias en isquemia miocárdica aguda

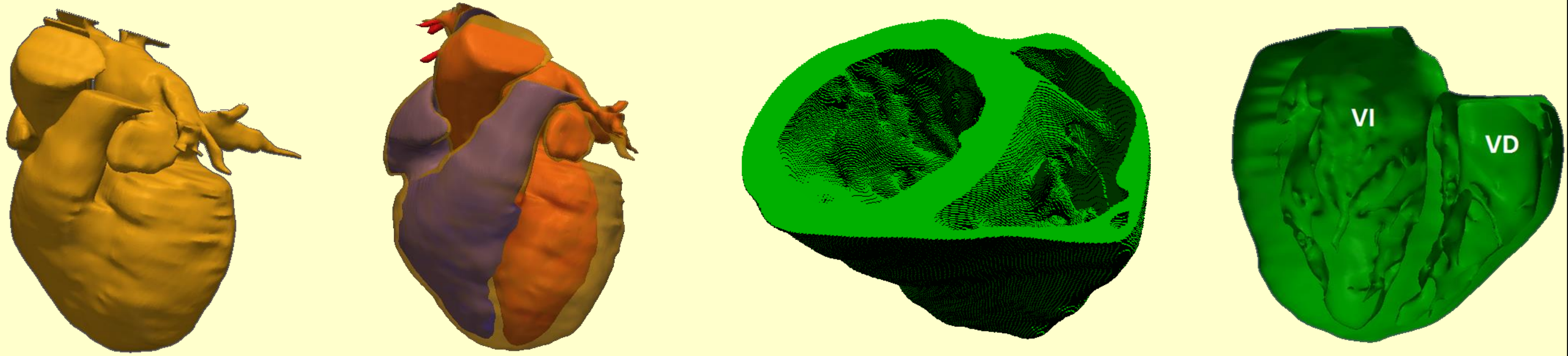
9.3.- Efecto de fármacos en arritmias en isquemia miocárdica aguda

9.4.- Terapia de ablación en infarto crónico

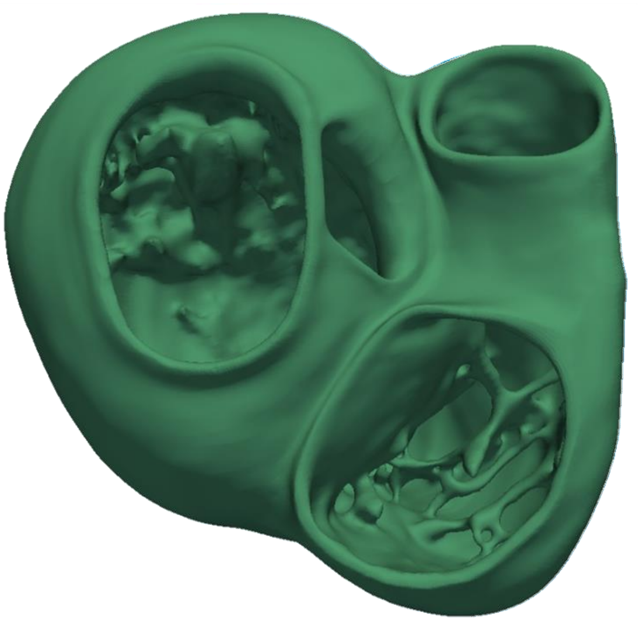
9.5.- Construcción de un modelo cardiaco 3D personalizado a paciente

9.6.- Mejora de la terapia de ablación en pacientes post-infarto mediante simulación

1. Cardiac geometry

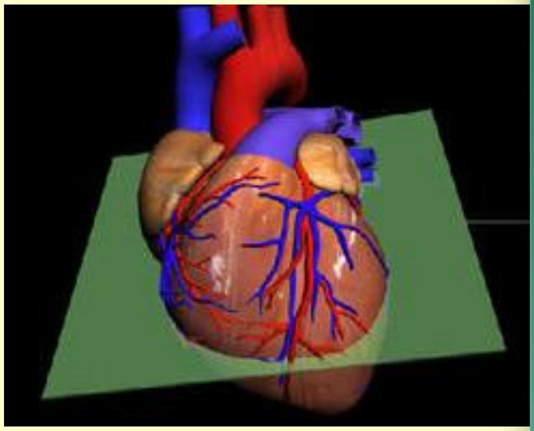


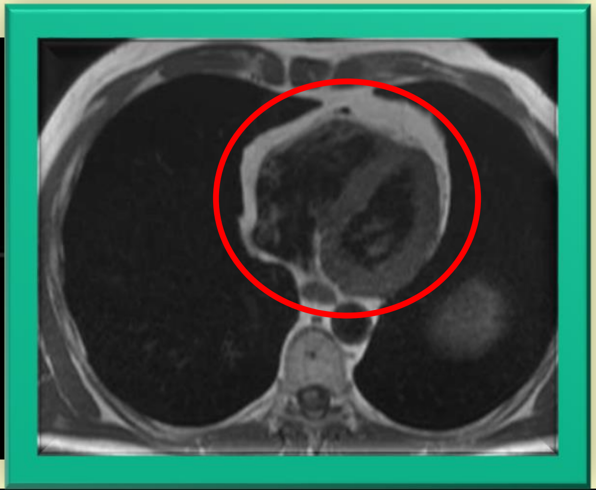
Detailed endocardium



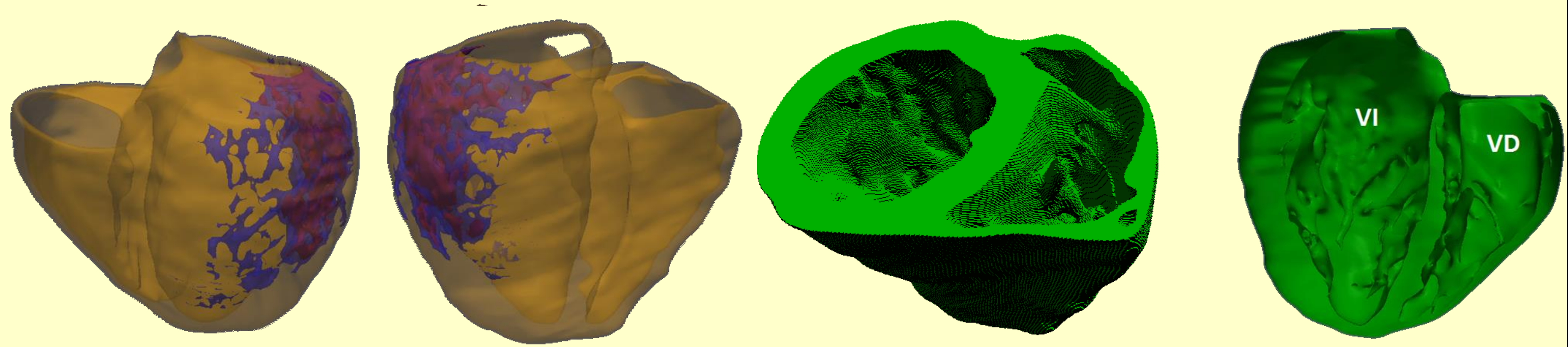
MRI images

Magnetic Resonance (MRI)

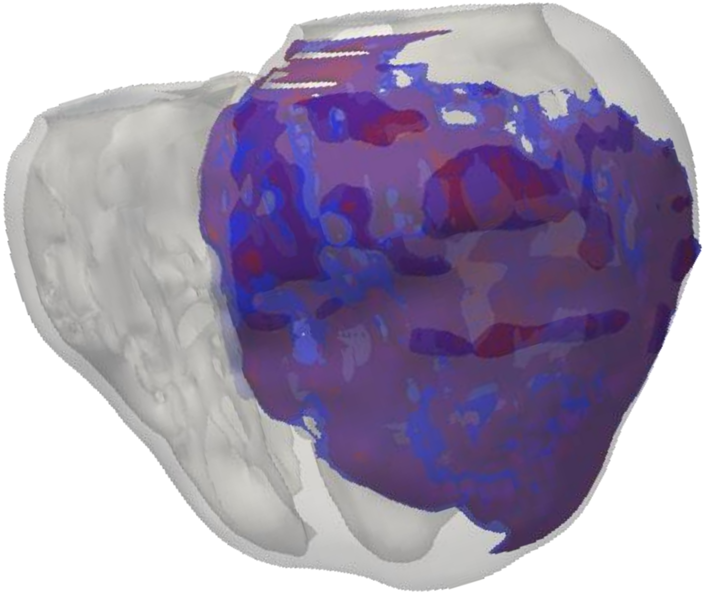




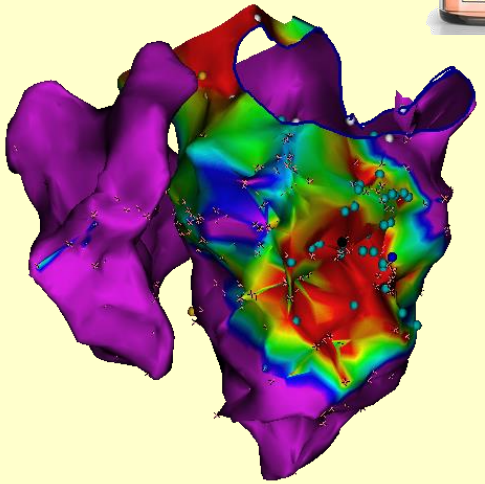
2. Infarct scar (core + border zone)



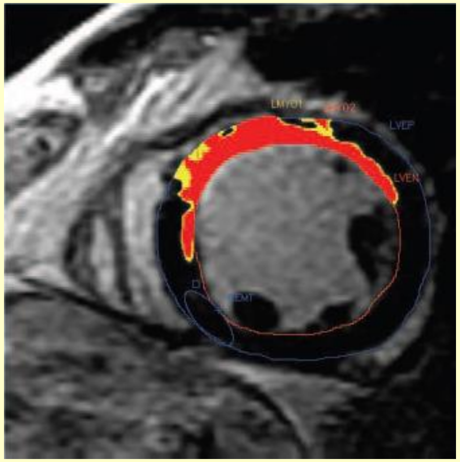
Infarct Scar



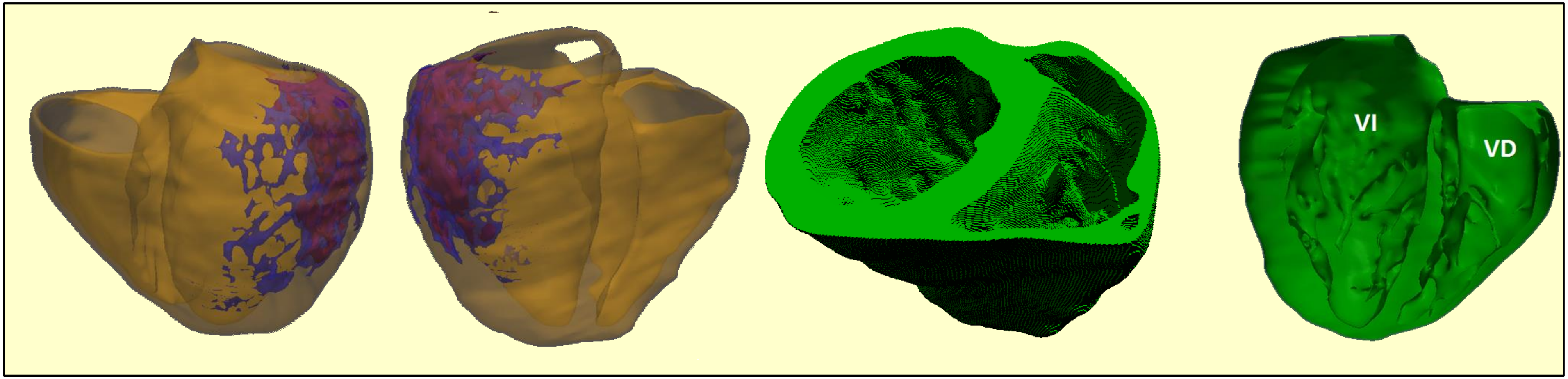
Electro-anatomical map (CARTO)



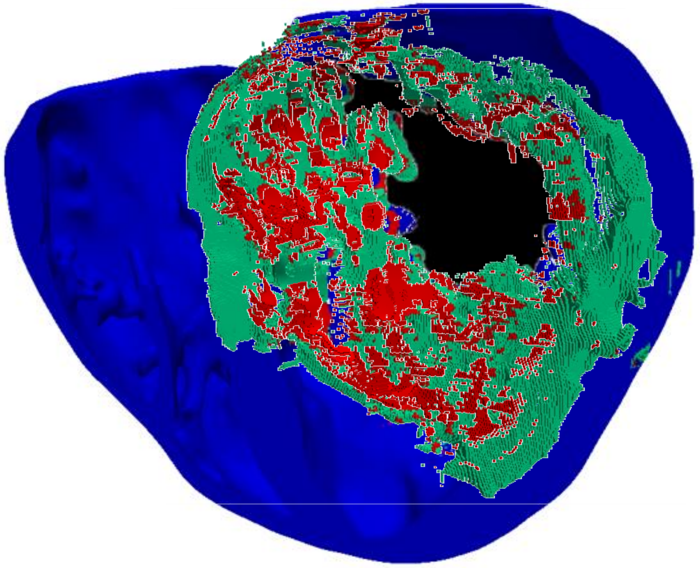
MRI images (Delayed Enhancement)



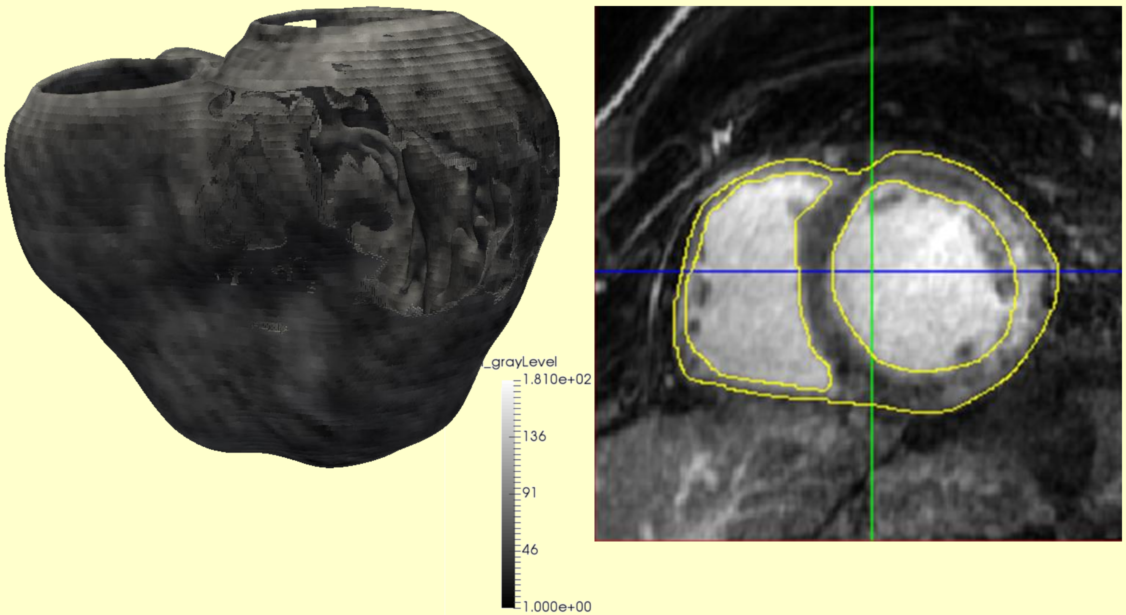
3. Fibrosis



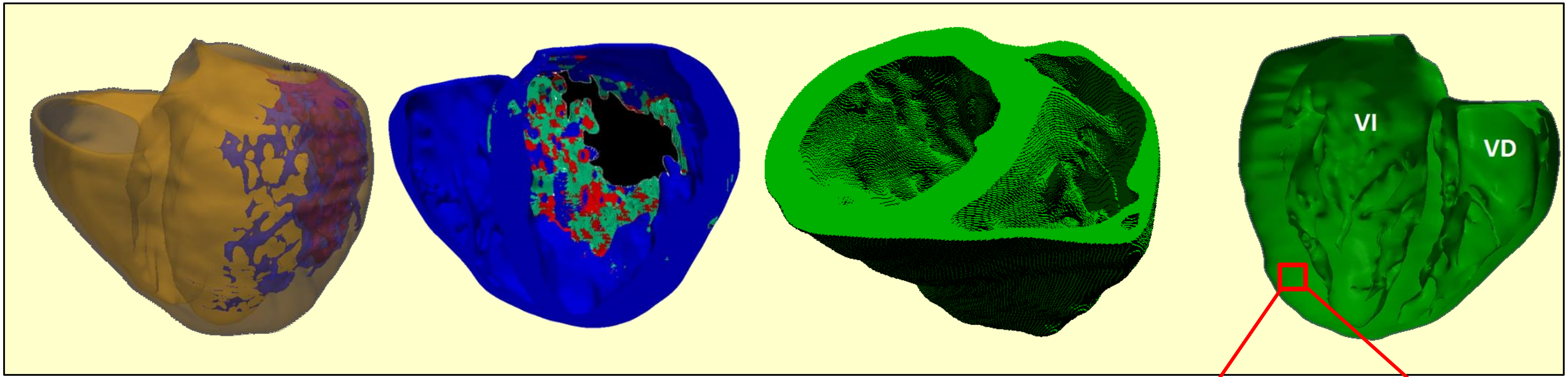
fibrosis



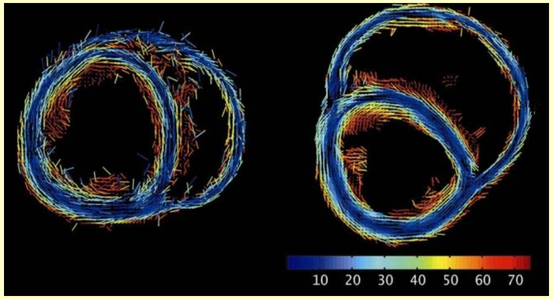
MRI images - grey level

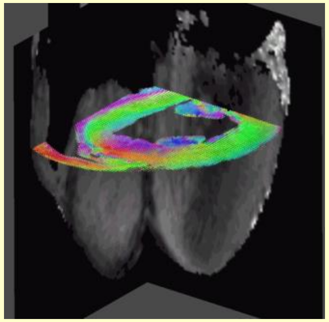


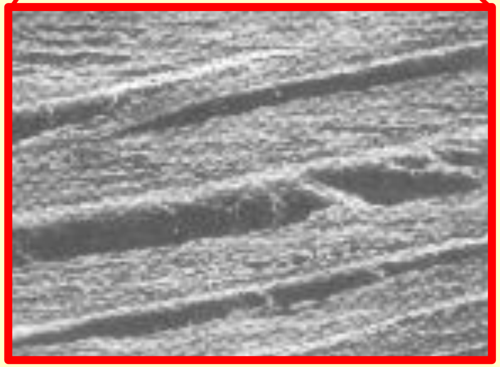
4. Myocardial structure (fiber orientation)



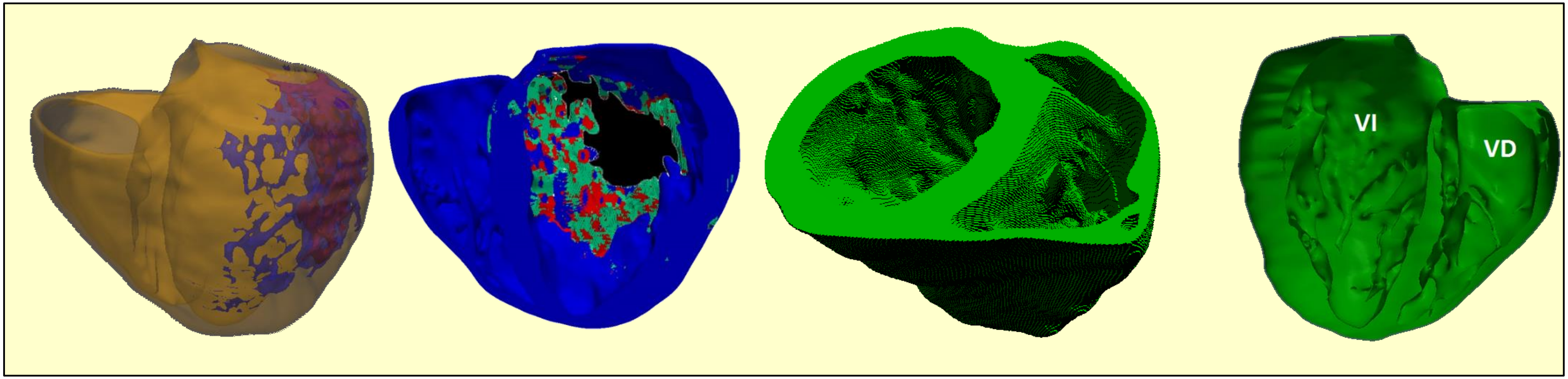
MRI-DTI (*Diffusion Tensor Imaging*)



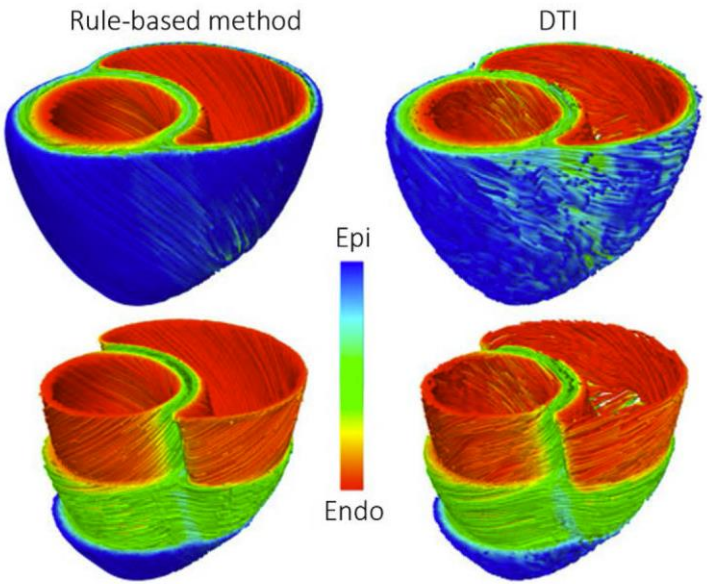




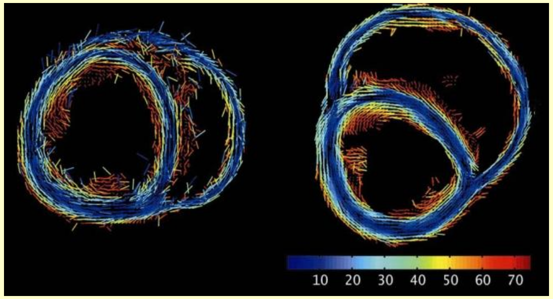
4. Myocardial structure (fiber orientation)

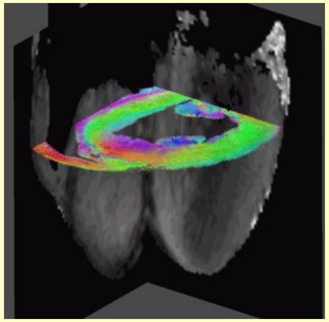


Fiber orientation estimation

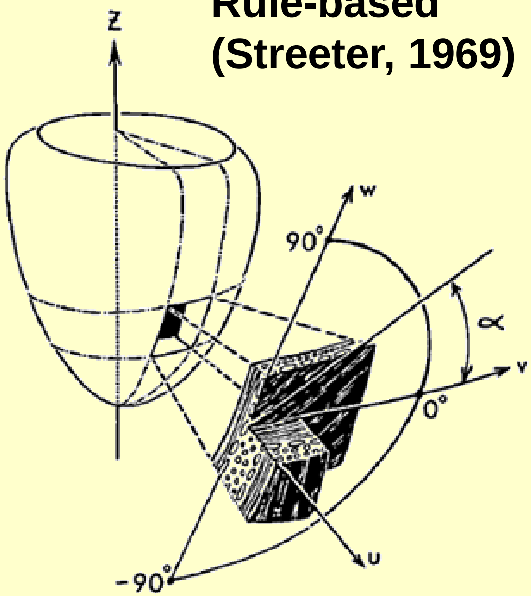


MRI-DTI (*Diffusion Tensor Imaging*)

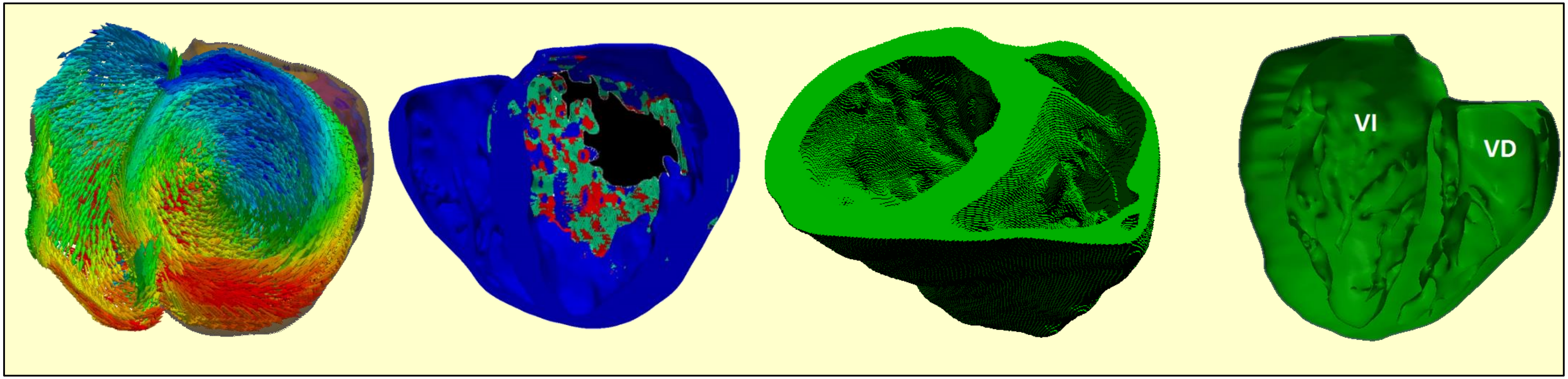




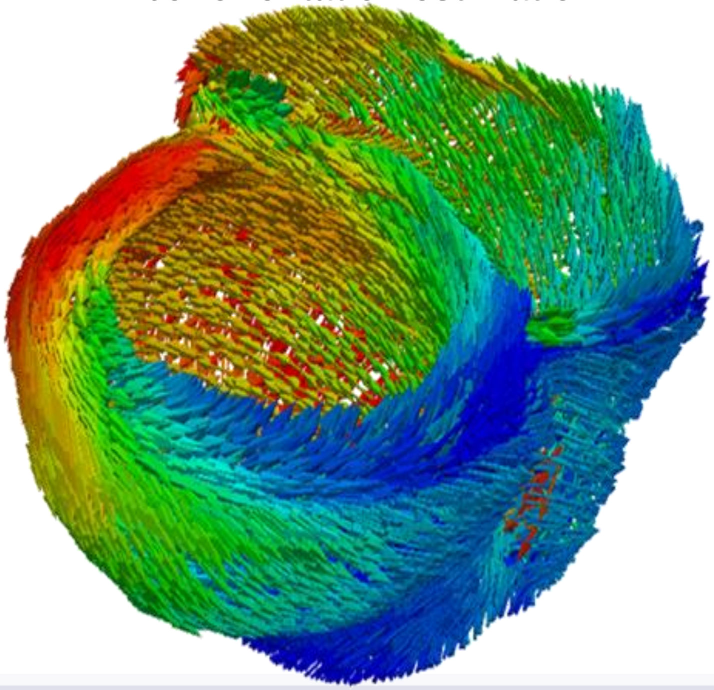
Rule-based (Streeter, 1969)



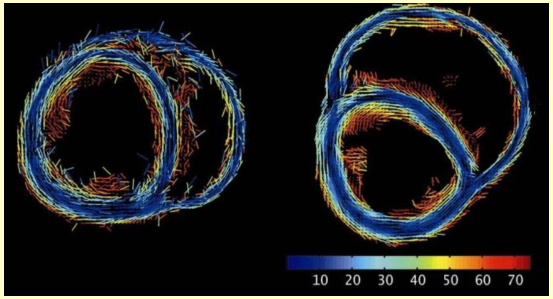
4. Myocardial structure (fiber orientation)

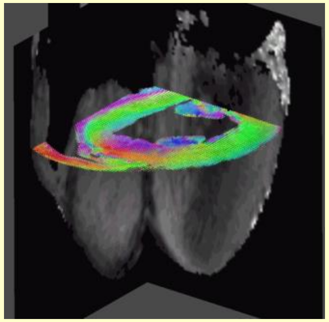


Fiber orientation estimation

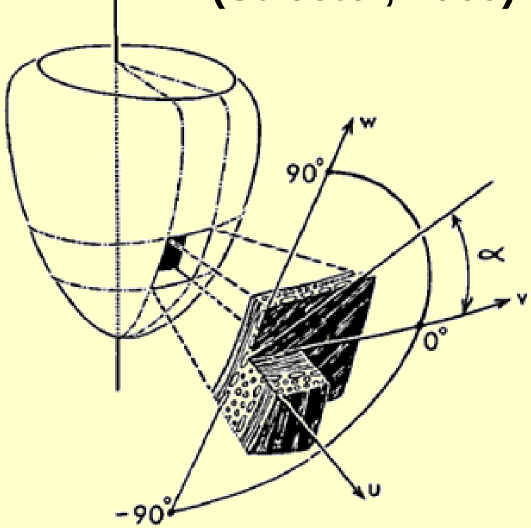


MRI-DTI (*Diffusion Tensor Imaging*)

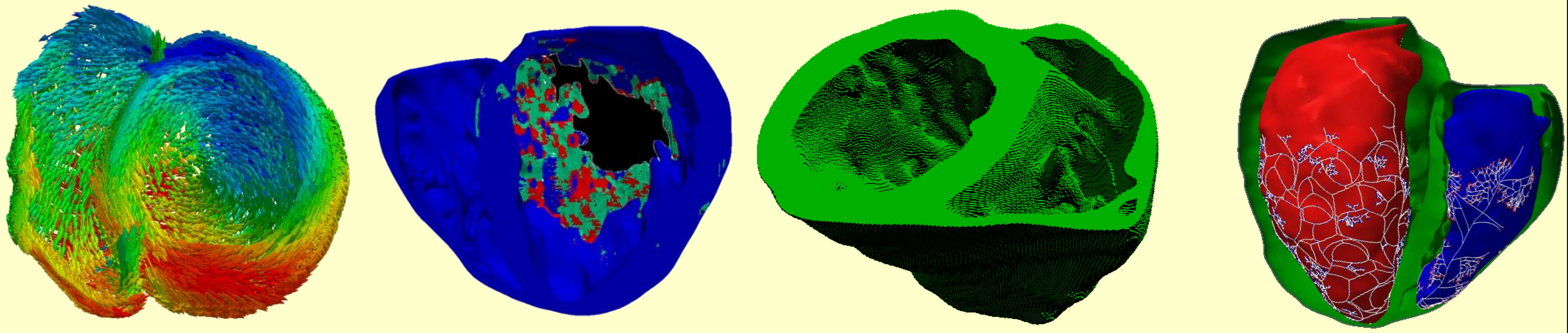




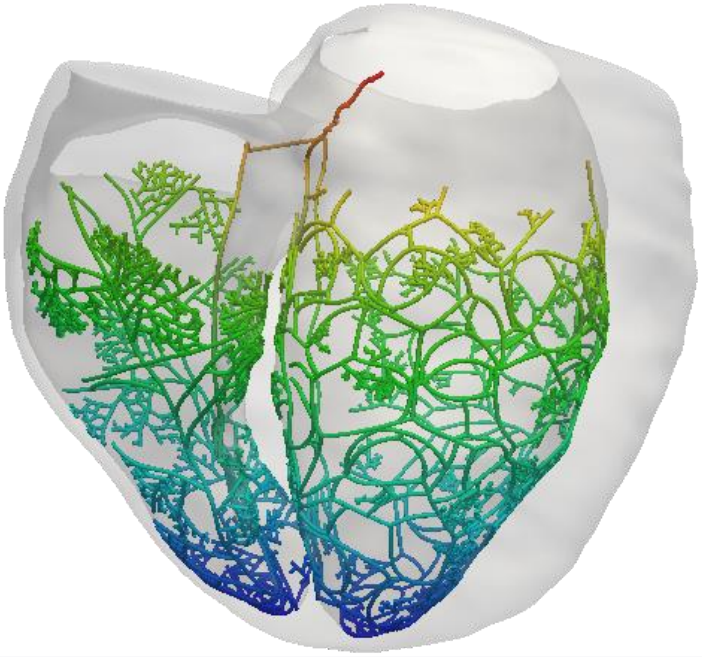
Rule-based (Streeter, 1969)



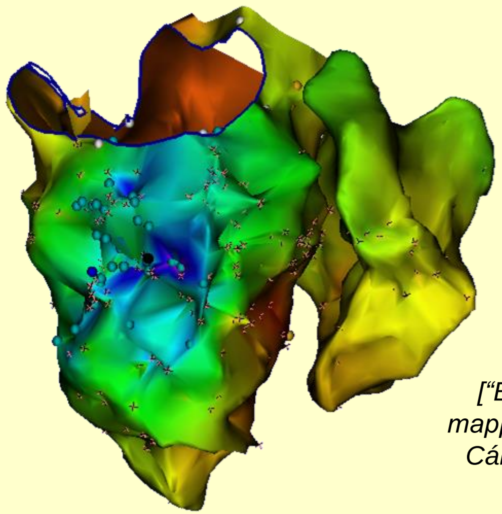
5. Cardiac conduction system (His-Purkinje)

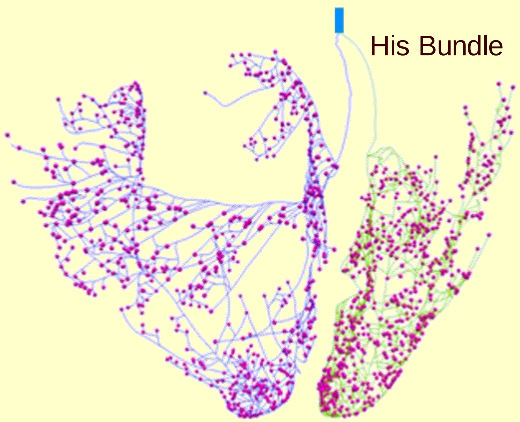


Inverse estimation of the Purkinje tree



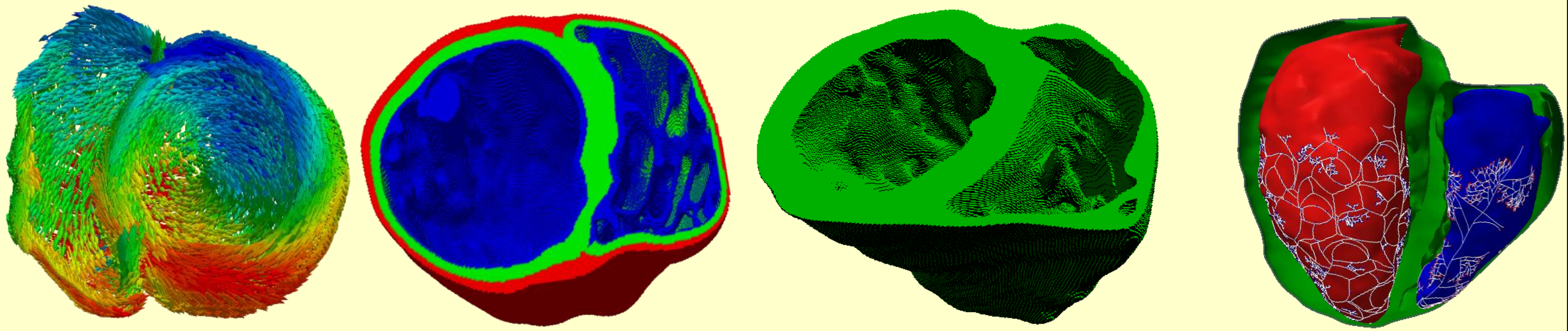
Electro-anatomical map (CARTO) [LAT]

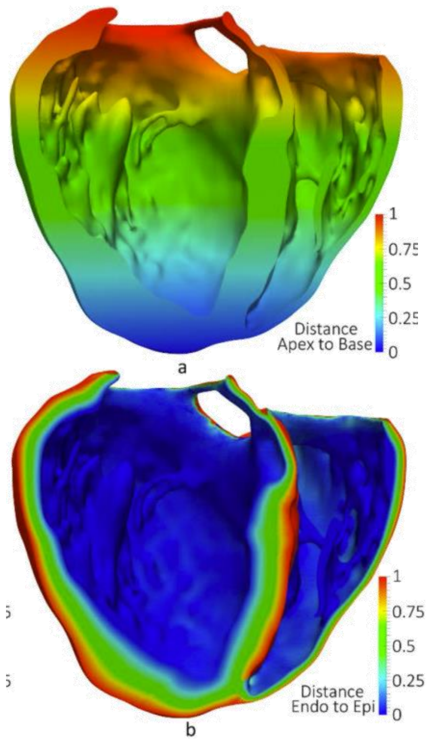




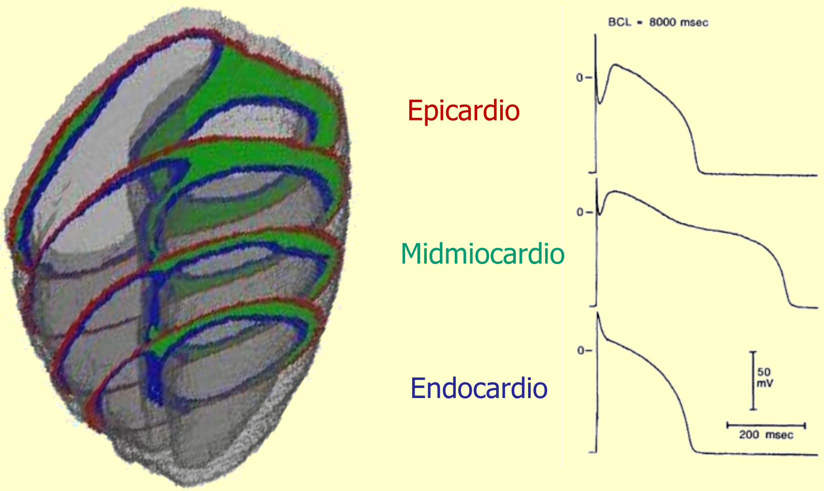
[“Estimation of Purkinje trees from electro-anatomical mapping of the left ventricle using minimal cost geodesics” Cárdenes, Sebastián, Soto, Berruezo & Cámara, 2015]

6. Electrophysiologic heterogeneity



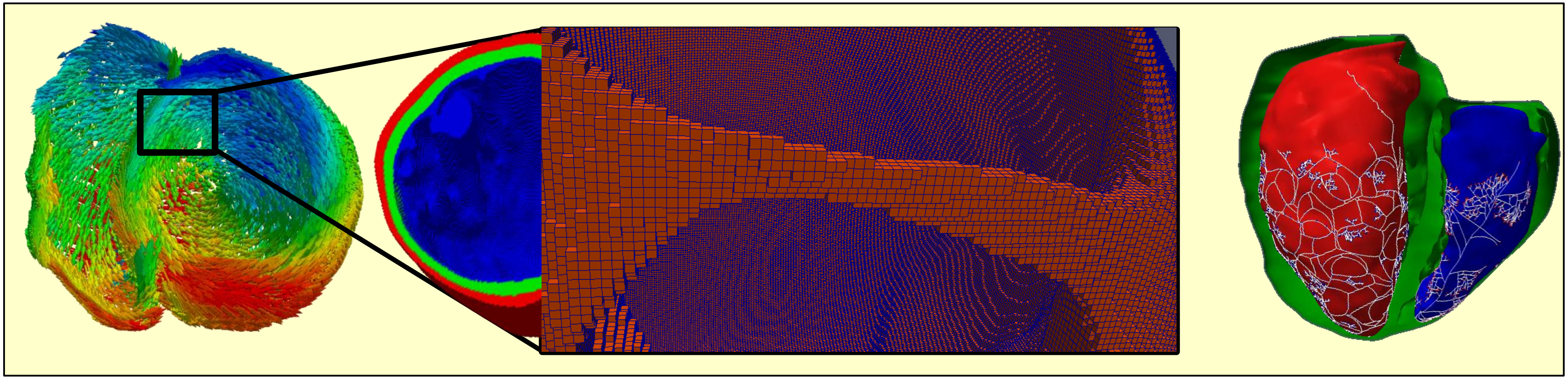


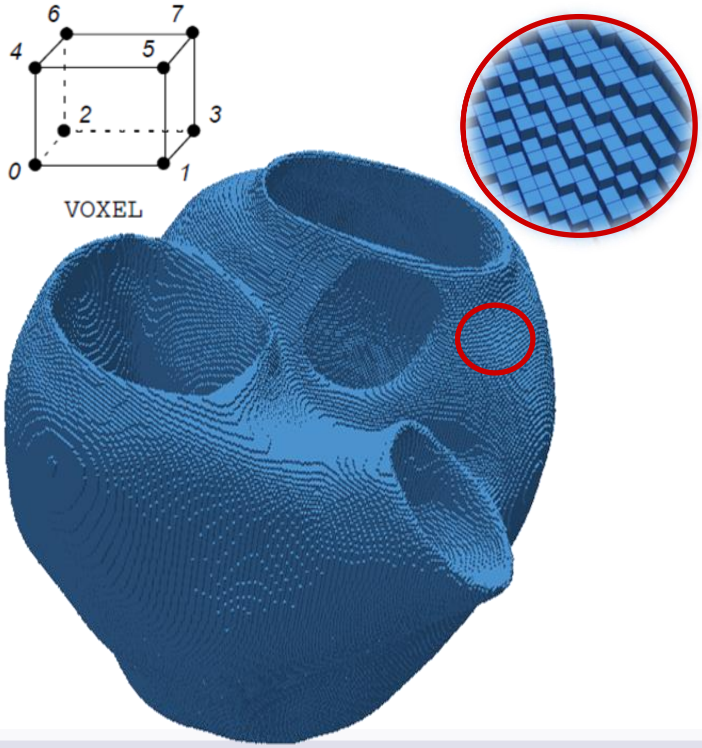
Transmural heterogeneity



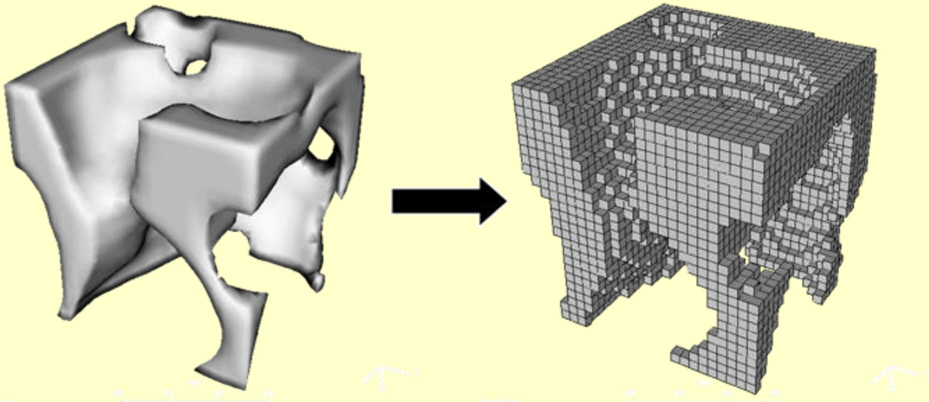
(Liu & Antzelevitch 1993)

Conversion to a computational model

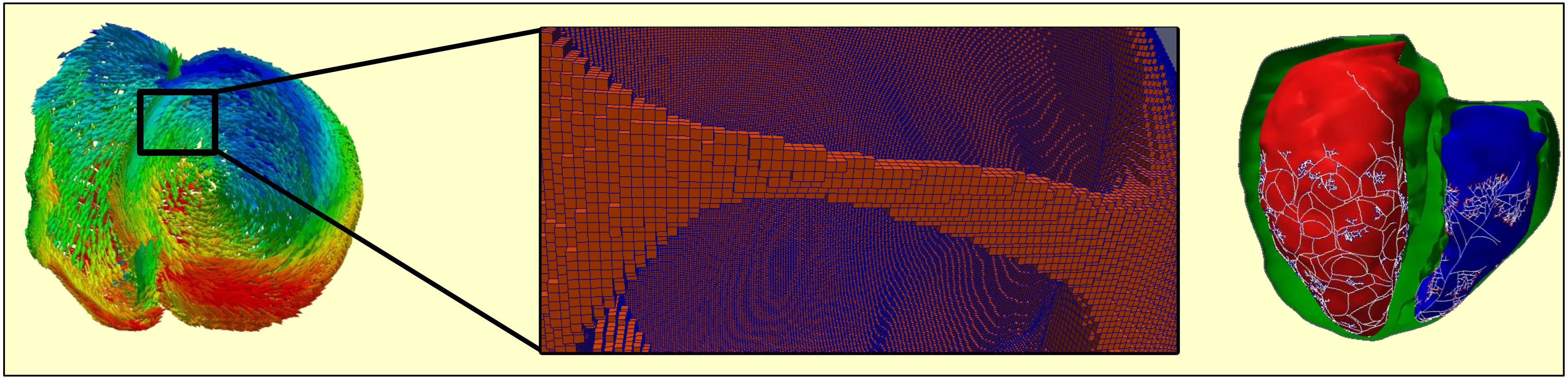


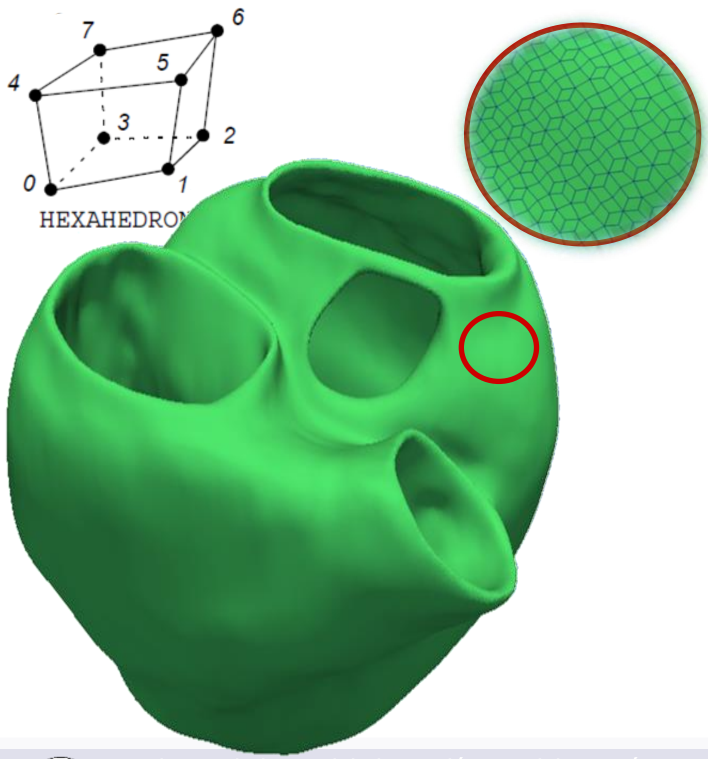


FEM meshing



Conversion to a computational model





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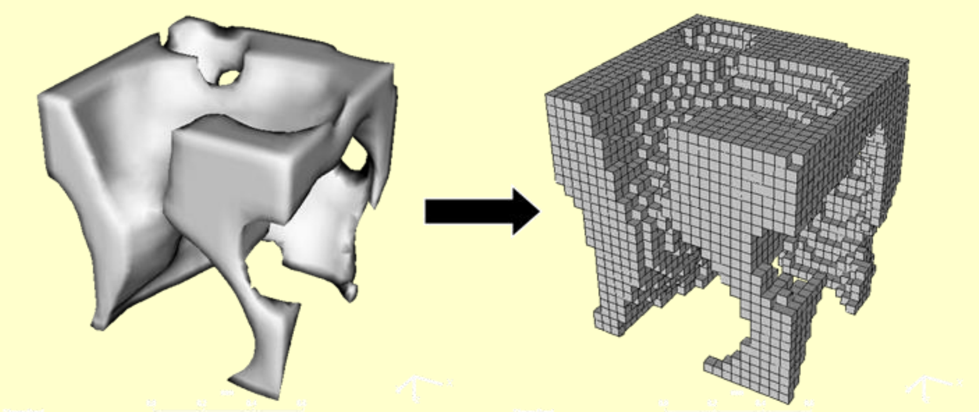
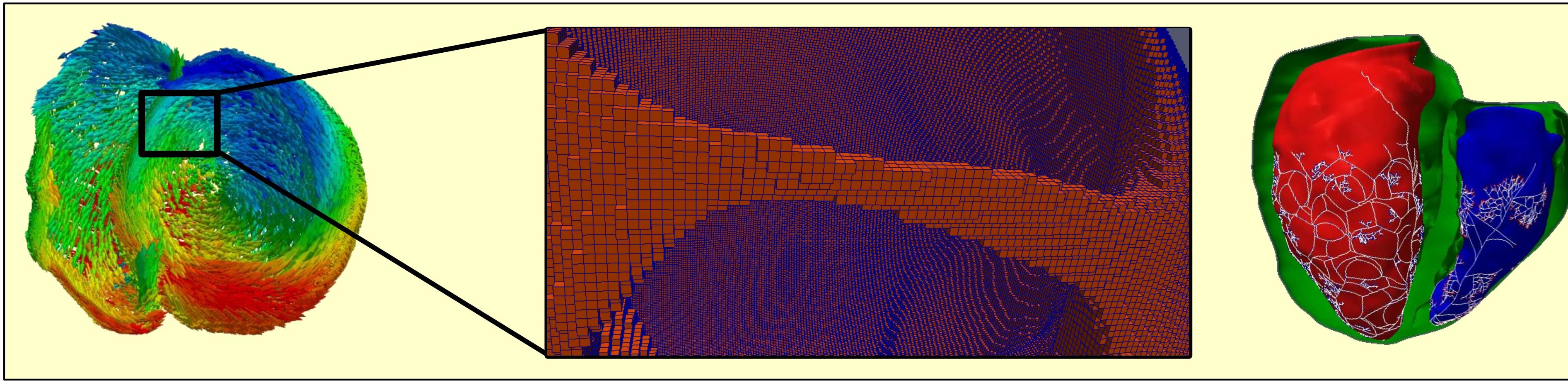
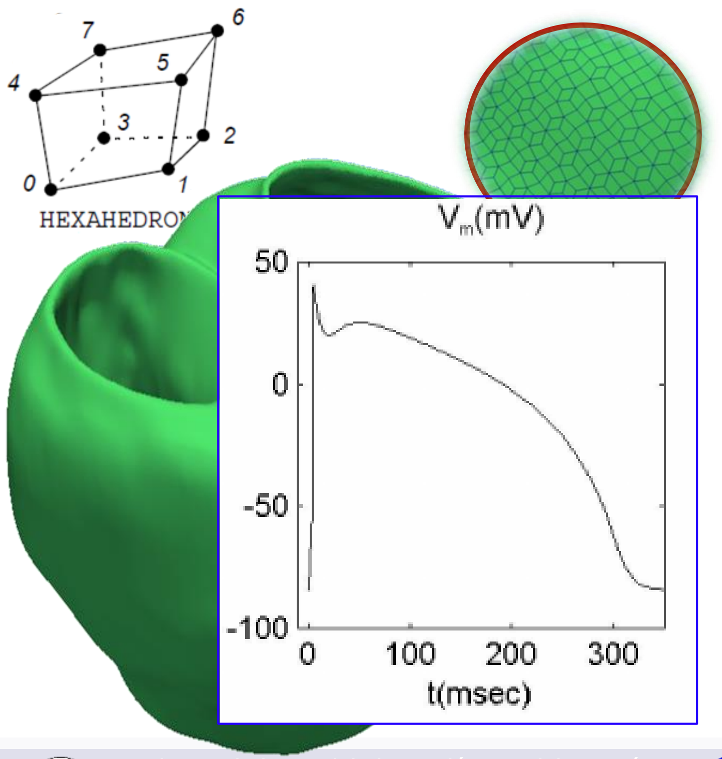


Conversion to a computational model





Propagation model

$$\frac{1}{(1+\beta)S_v}\nabla\cdot\left(\overline{\overline{\sigma}}_i\,\nabla V_m\right)=C_m\frac{\partial V_m}{\partial t}+\sum_S I_S$$

Action potential and ionic current model

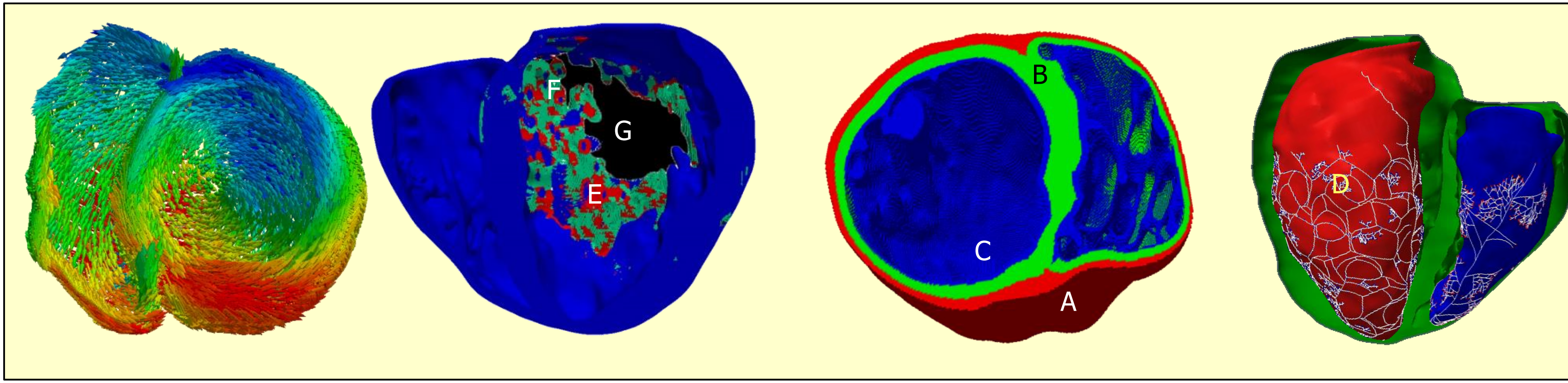
ionic currents $I_S(t)=g_S\left(V_m-E_S\right)$

ionic conductances $g_S(t)=G_S\;f_{S1}(t)\,f_{S2}(t)\ldots f_{Sn_S}(t)$

channel gates $\dfrac{df_k}{dt}=\dfrac{f_{k\infty}(V_m)-f_k(t)}{\tau_{fk}(V_m)}\qquad k=1\ldots n$

ionic concentrations $\dfrac{d[S]_i}{dt}=\dfrac{1}{Fv_i}\sum_n I_{S,n}(t)\quad (S:Na^+,K^+,Ca^{2+},Cl^-)$

Conversion to a computational model



Action potential models

A. Healthy EPI: O'Hara et al., 2011

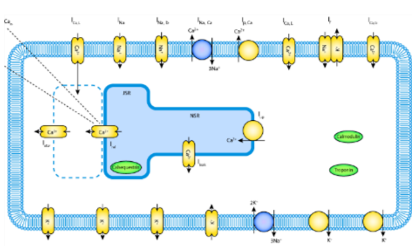
B. Healthy M-cells: O'Hara et al., 2011

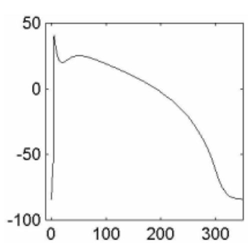
C. Healthy ENDO: O'Hara et al., 2011

D. Purkinje fib.: Stewart et al., 2009

E. Border zone: modified Ten Tuscher et al., 2006

F. Fibroblasts: MacCannel et al., 2007





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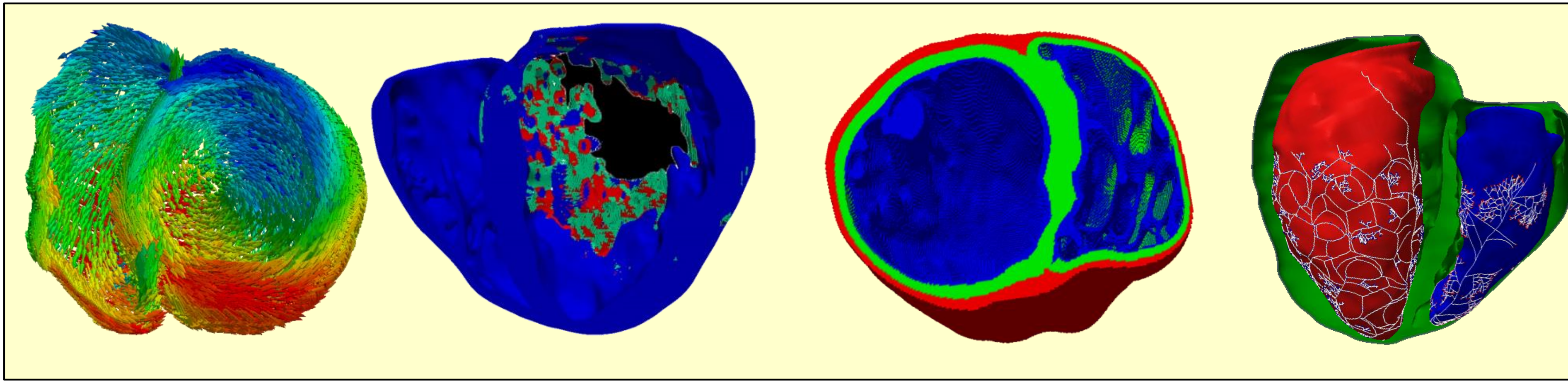
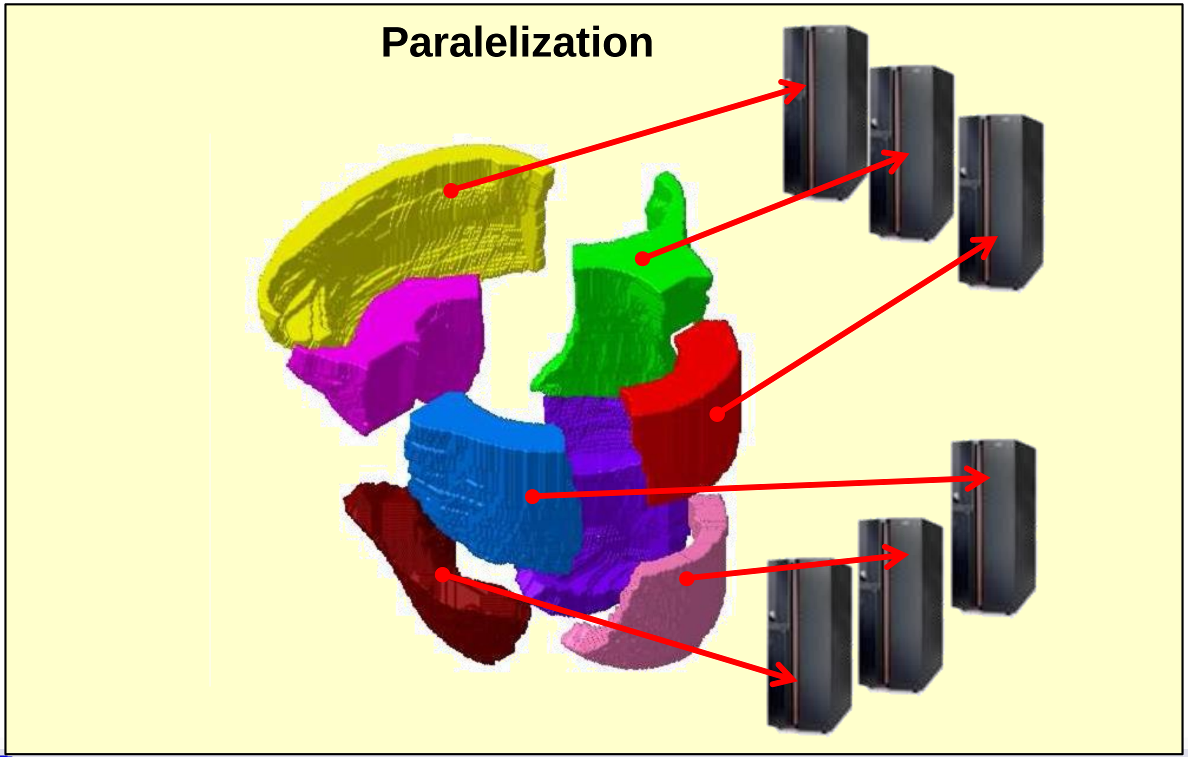
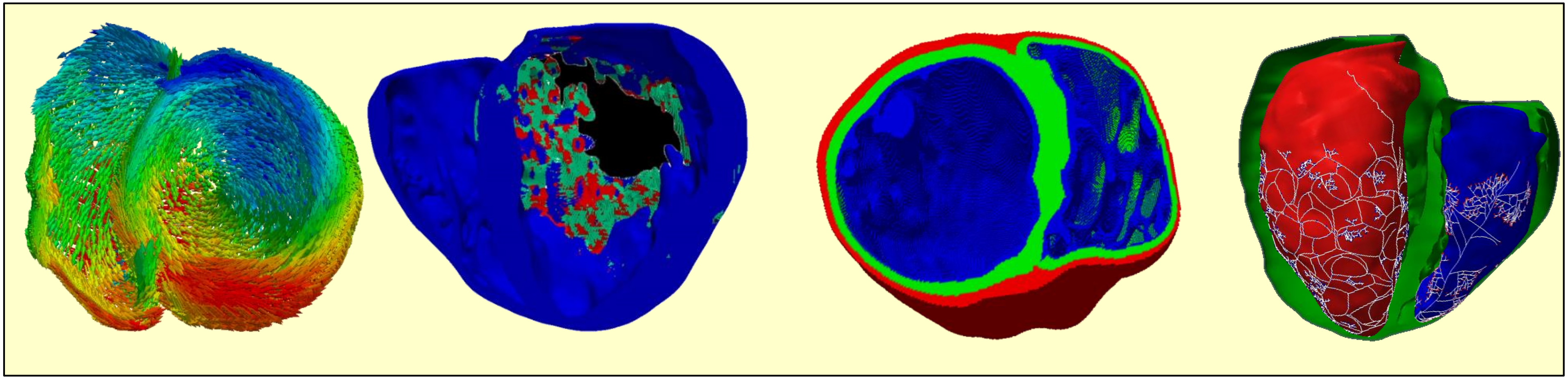
Conversion to a computational model

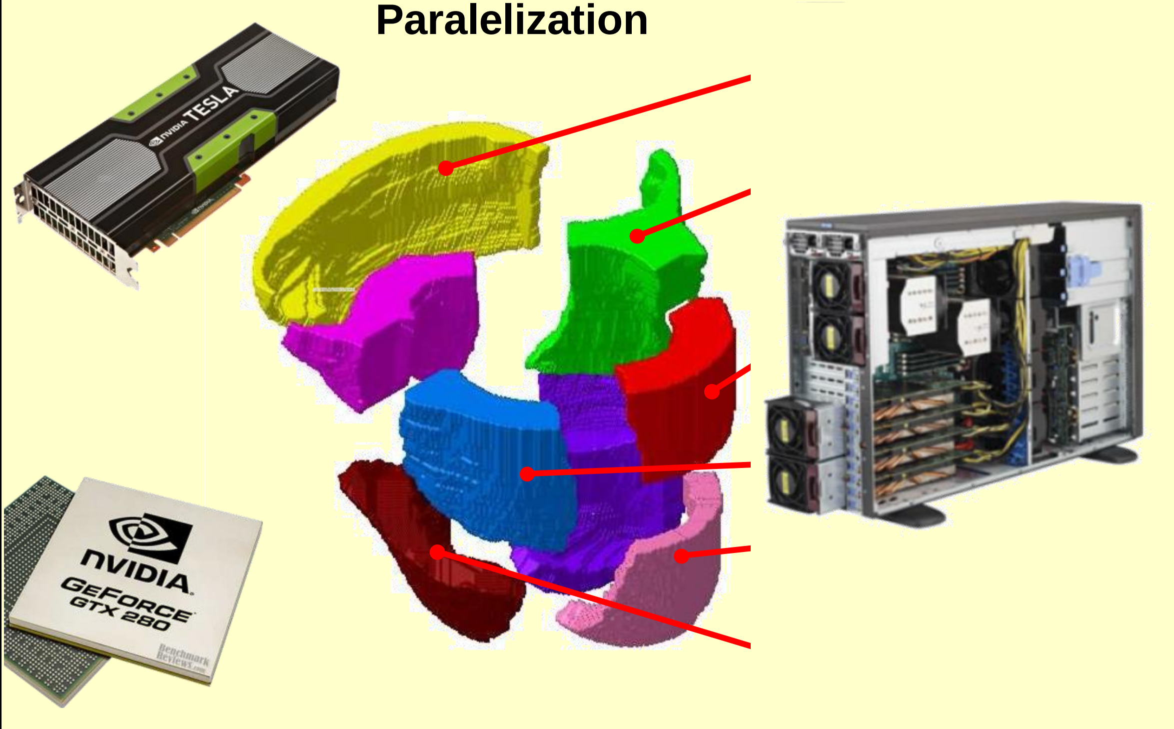




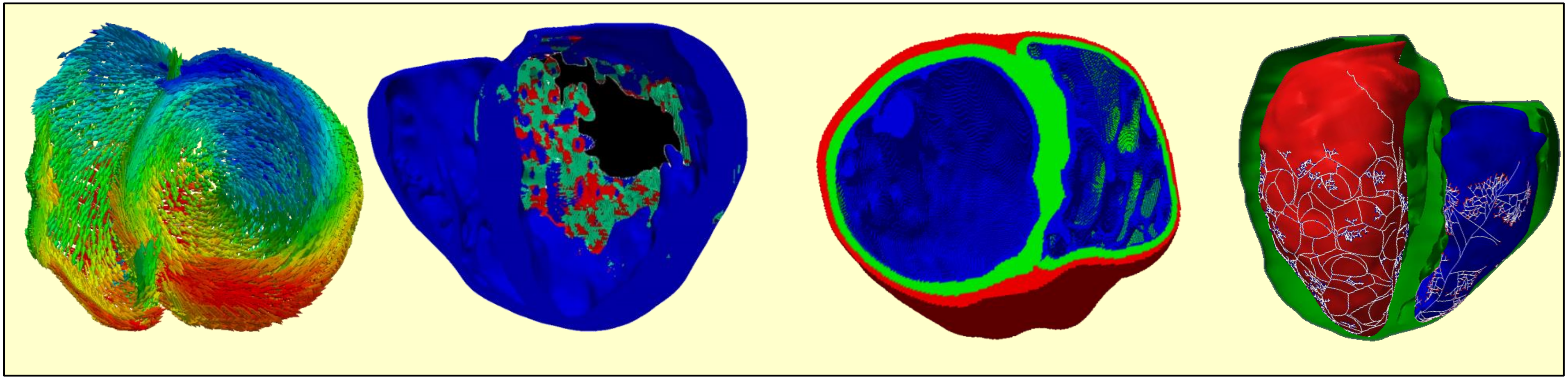
Conversion to a computational model



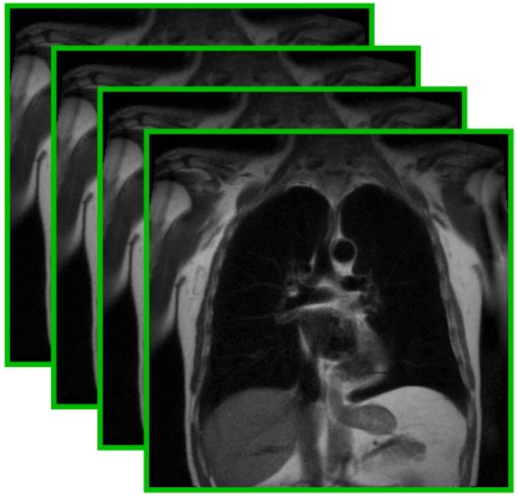
Paralelization

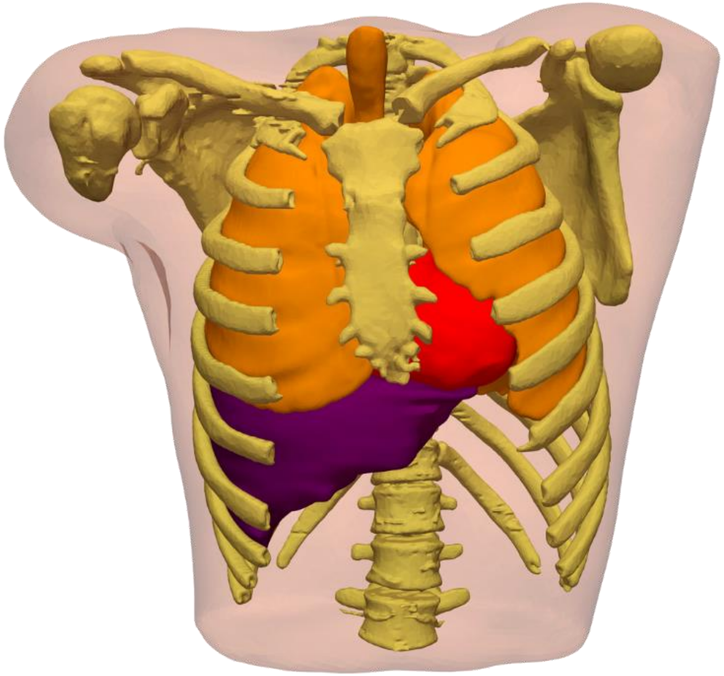


Embedding the heart in a torso model



MRI





Tema 9

9.1.- Fundamentos bioeléctricos de las arritmias por reentrada

9.2.- Simulación computacional de arritmias en isquemia miocárdica aguda

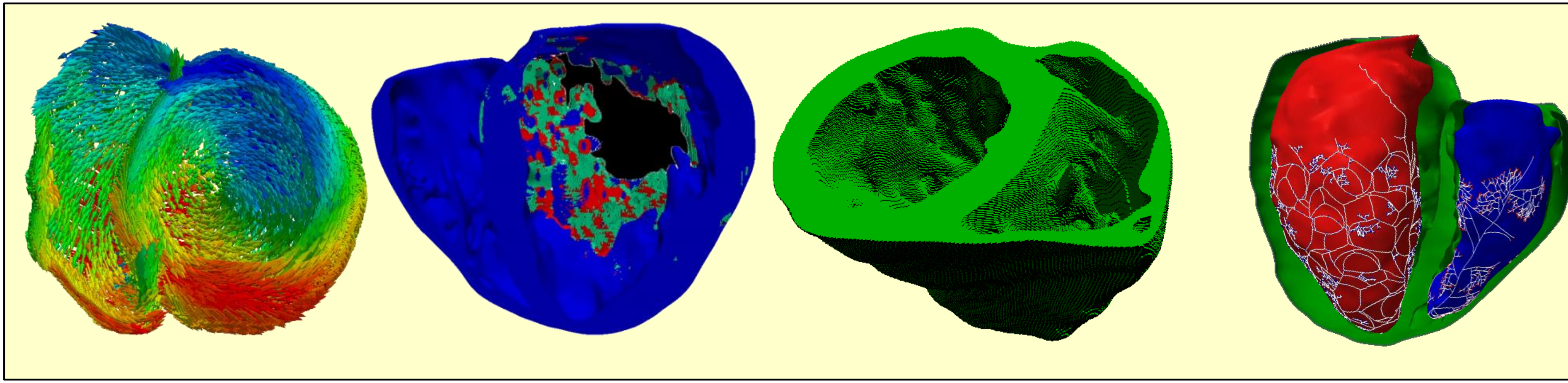
9.3.- Efecto de fármacos en arritmias en isquemia miocárdica aguda

9.4.- Terapia de ablación en infarto crónico

9.5.- Construcción de un modelo cardiaco 3D personalizado a paciente

9.6.- Mejora de la terapia de ablación en pacientes post-infarto mediante simulación

Simulating the Ventricular Tachycardia



ECG

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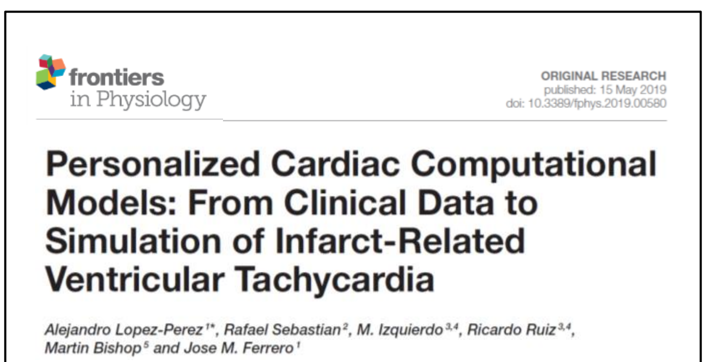

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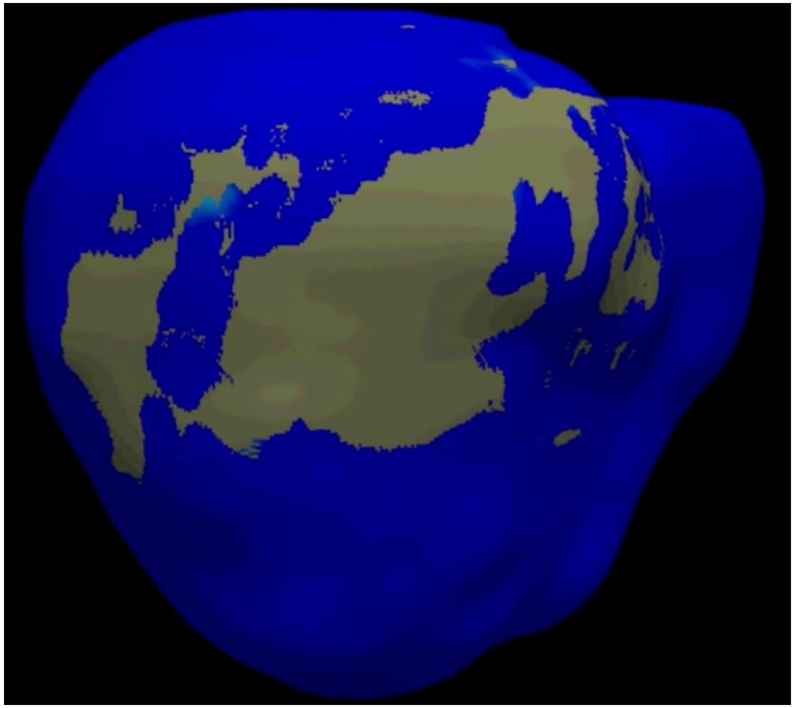
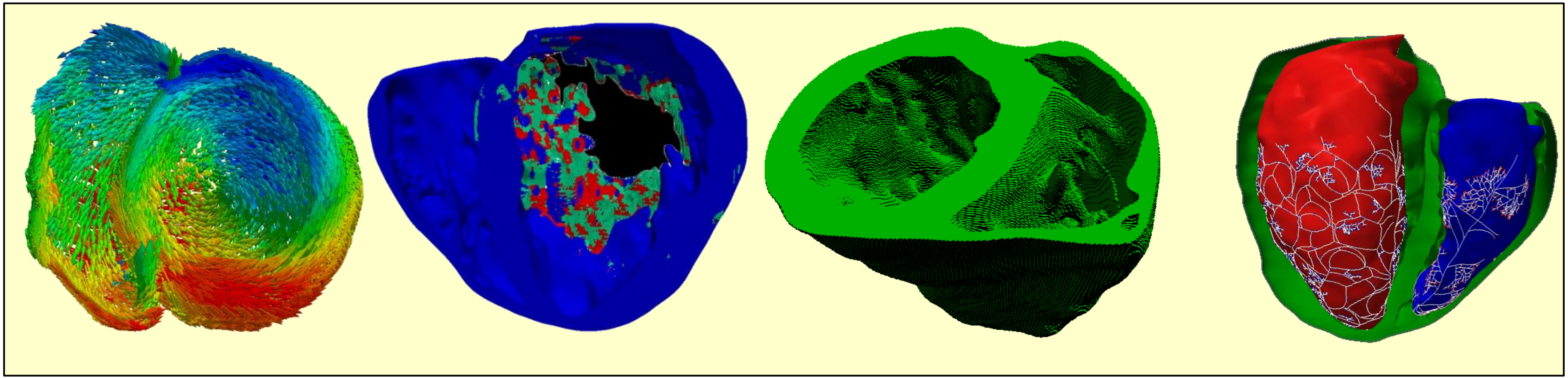
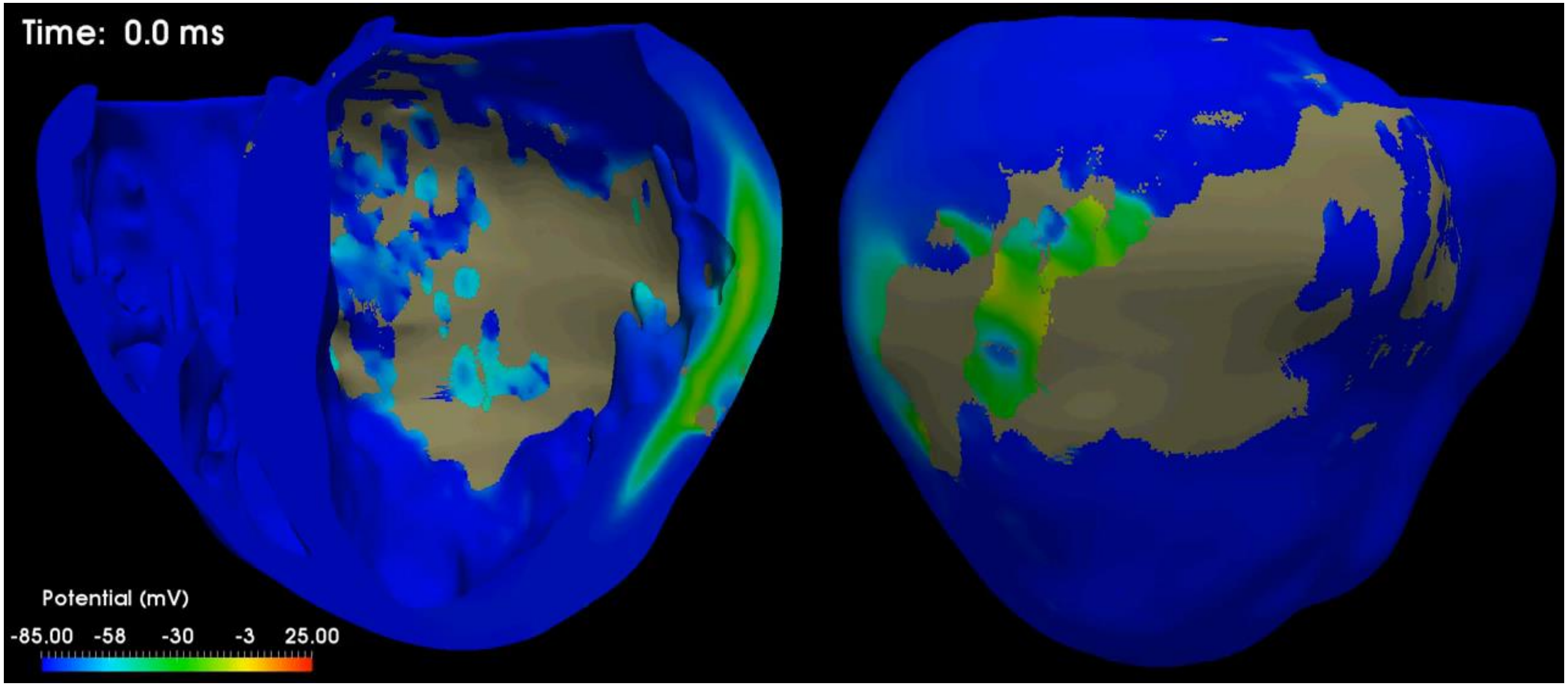


Simulating the Ventricular Tachycardia





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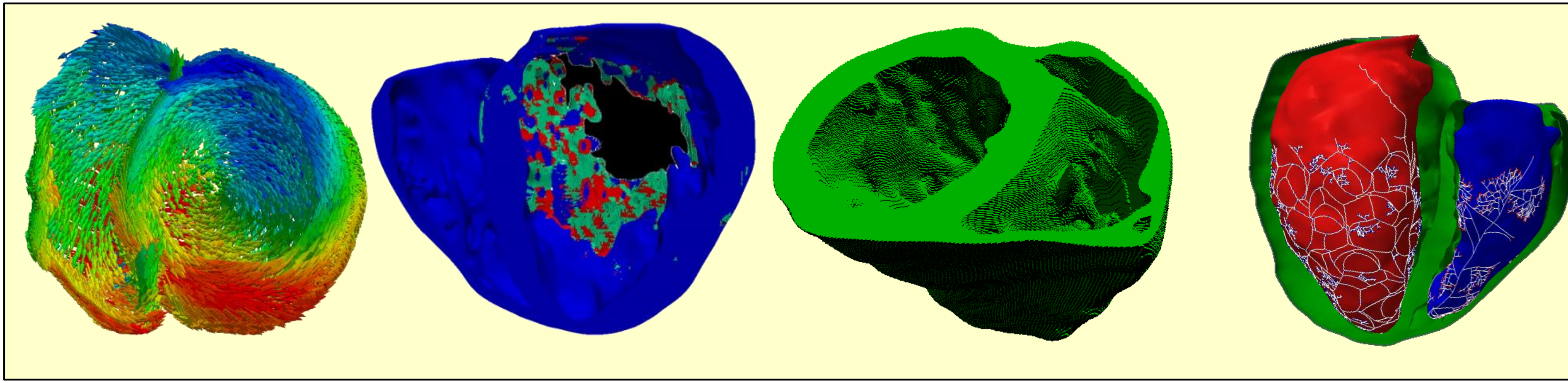

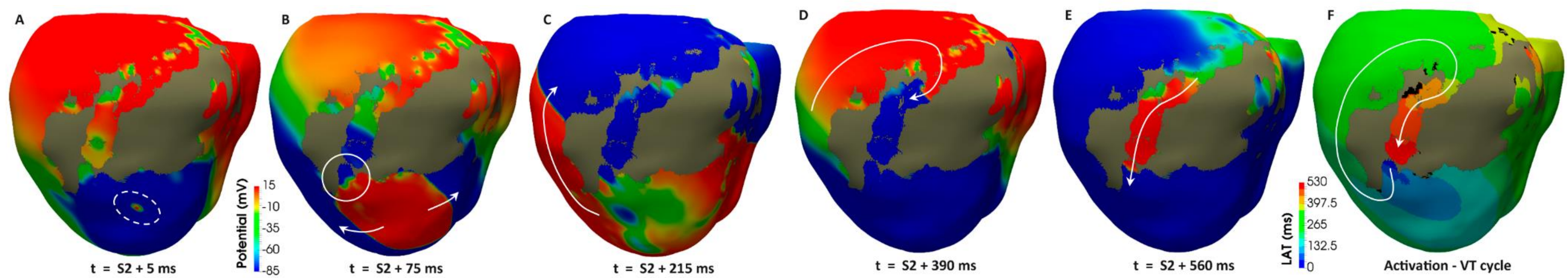

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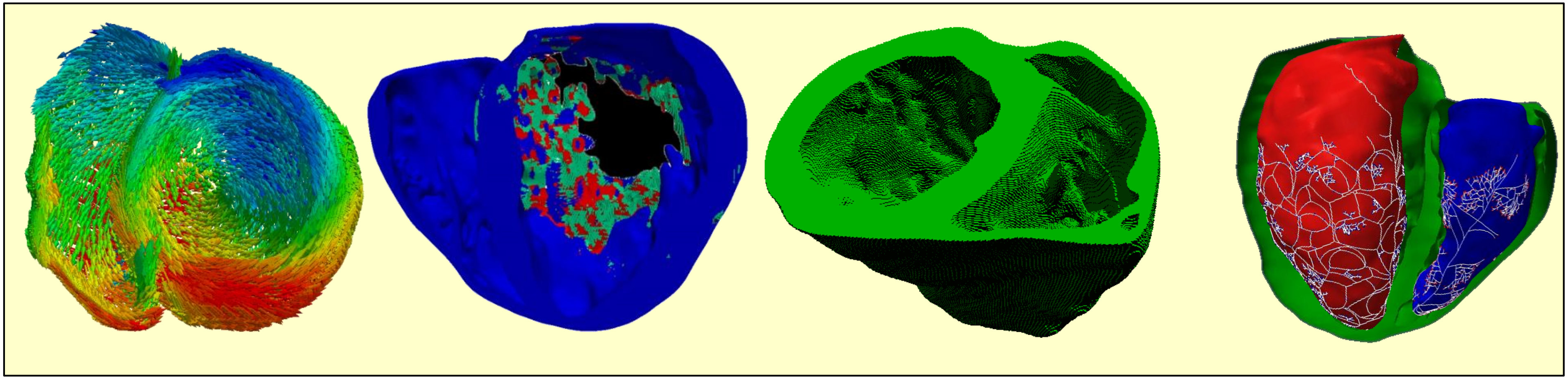

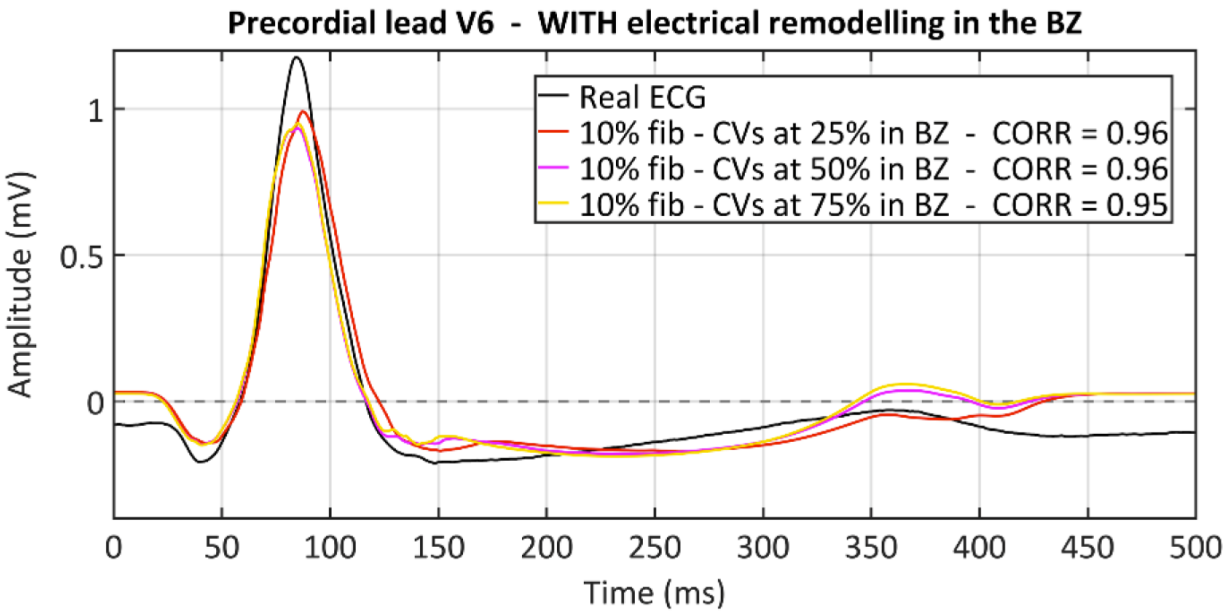

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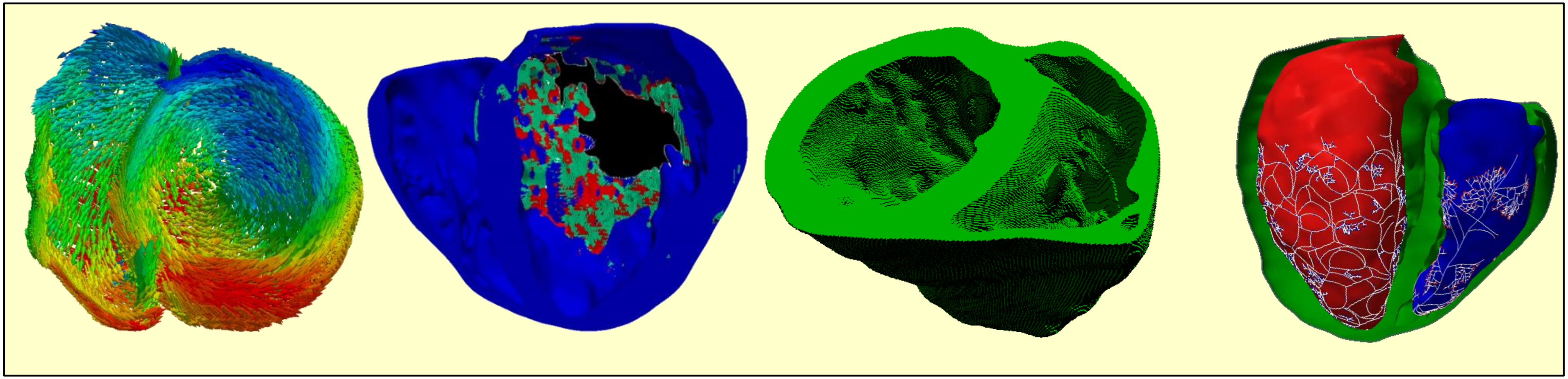
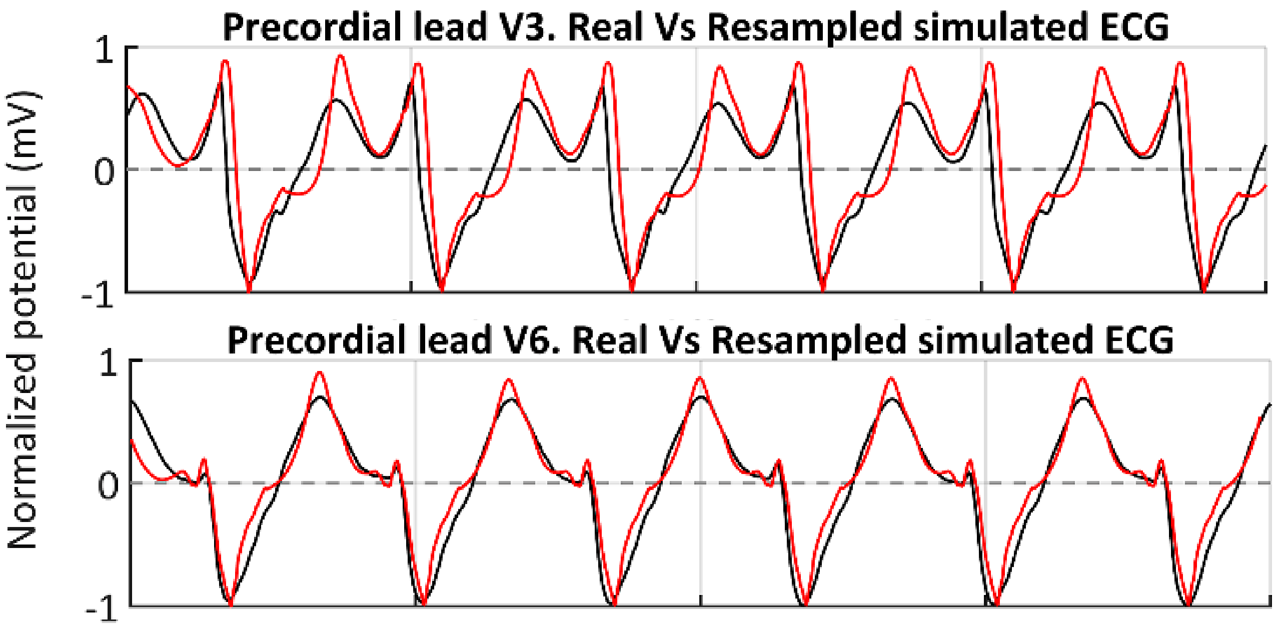
Simulating the Ventricular Tachycardia





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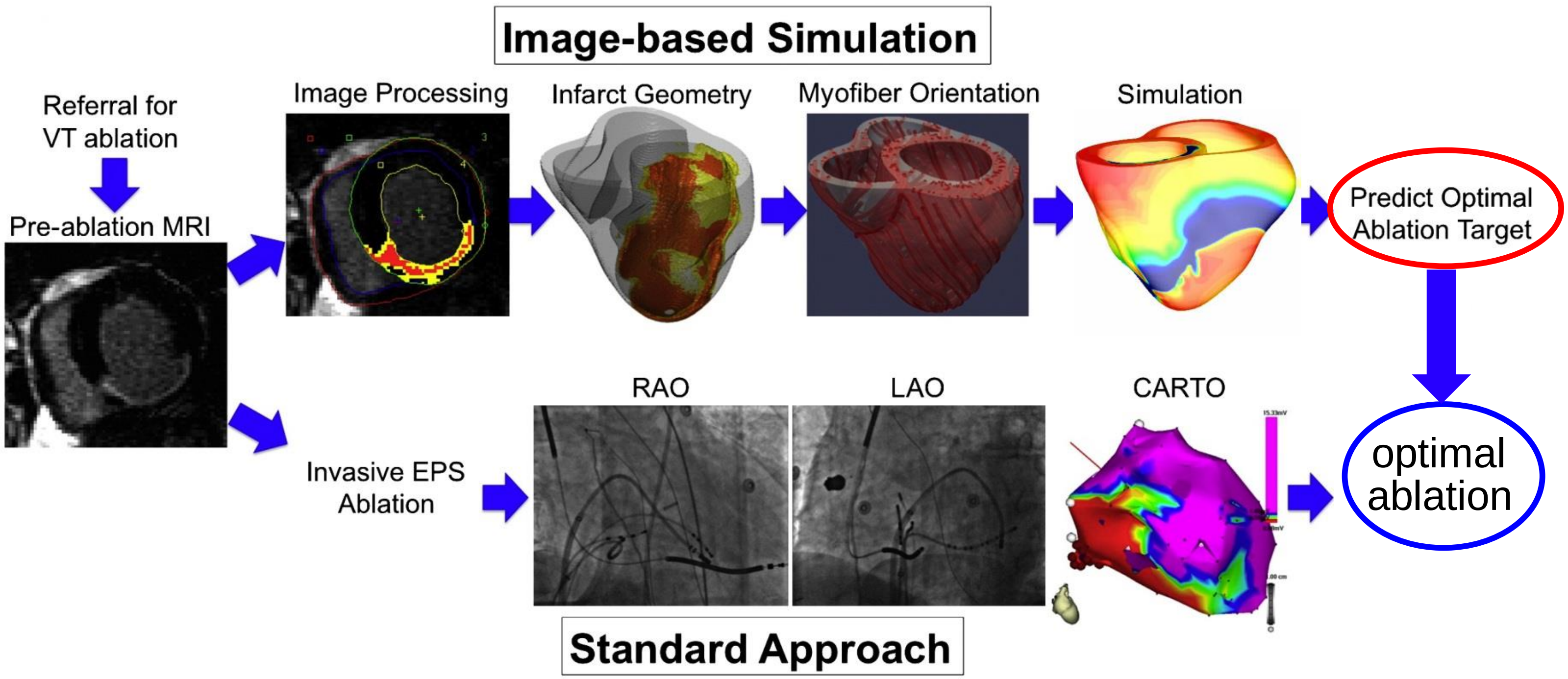
Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

... not science fiction :-)



References

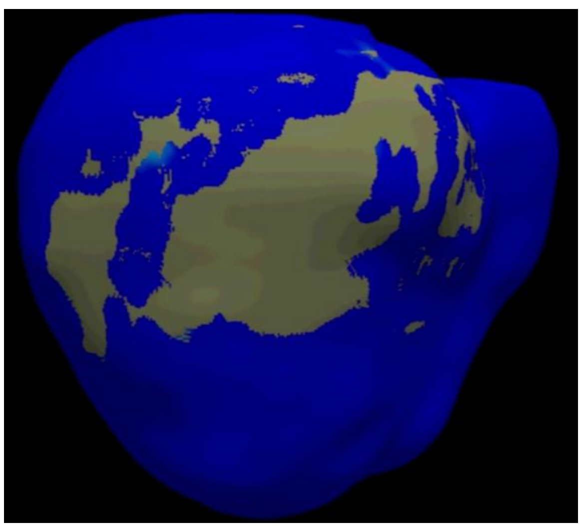
Lopez-Perez *et al. BioMedical Engineering OnLine* (2015) 14:35
DOI 10.1186/s12938-015-0033-5

BioMedical Engineering OnLine

REVIEW **Open Access**

Three-dimensional cardiac computational modelling: methods, features and applications

Alejandro Lopez-Perez[1*], Rafael Sebastian[2] and Jose M Ferrero[1]



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Bibliografía

- Ferrero JM, Trénor B & Romero L, “Multiscale computational analysis of the bioelectric consequences of myocardial ischaemia and infarction”, European Journal of Pacing, Arrhythmias and Cardiac Electrophysiology (Europace) 2014 Mar;16(3):405-15.
- Moréna H, Janse MJ, Fiolet JW, Krieger WJ, Crijns H, Durrer D, “Comparison of the effects of regional ischemia, hypoxia, hyperkalemia, and acidosis on intracellular and extracellular potentials and metabolism in the isolated porcine heart”, Circ Res. 1980 May;46(5):634-46
- Janse MJ, Kleber AG, “Electrophysiological changes and ventricular arrhythmias in the early phase of regional myocardial ischemia”, Circ Res. 1981 Nov;49(5):1069-81
- Cascio WE, “Myocardial ischemia: what factors determine arrhythmogenesis?”, J Cardiovasc Electrophysiol. 2001 Jun;12(6):726-9.
- Clayton RH, Holden AV, “Dispersion of cardiac action potential duration and the initiation of re-entry: a computational study”, Biomed Eng Online. 2005 Feb 18;4(1):11.
- Ferrero JM Jr, Sáiz J, Ferrero JM, Thakor NV, “Simulation of action potentials from metabolically impaired cardiac myocytes. Role of ATP-sensitive K+ current”, Circ Res. 1996 Aug;79(2):208-21.
- Rodriguez B & Ferrero (Jr) JM, “Mechanistic investigation of extracellular K+ accumulation during acute myocardial ischemia: a simulation study”, Am J Physiol Heart Circ Physiol. 2002 Aug;283(2):H490-500.
- Weiss JN, Venkatesh N, Lamp ST, “ATP-sensitive K+ channels and cellular K+ loss in hypoxic and ischaemic mammalian ventricle”, J Physiol. 1992 Feb;447:649-73.
- Kléber AG, Janse MJ, van Capelle FJ, Durrer D, “Mechanism and time course of S-T and T-Q segment changes during acute regional myocardial ischemia in the pig heart determined by extracellular and intracellular recordings”, Circ Res. 1978 May;42(5):603-13.

Bibliografía

- JF Rodriguez, EA Heidenreich, L Romero, JM Ferrero (Jr), M Doblare, “Post-Repolarization Refractoriness in Human Ventricular Cardiac Cells”, Computers in Cardiology 2008 35:581-584.
- Ferrero (Jr) JM; Saiz J; Ferrero (Sr) JM; Thakor NV, “Postrepolarization refractoriness in ventricular cardiac cells: a simulation study”, Computers in Cardiology 1999 26:487-490
- Downar E, Janse MJ, Durrer D, “The effect of "ischemic" blood on transmembrane potentials of normal porcine ventricular myocardium”, Circulation. 1977 Mar;55(3):455-62
- Coronel R, Fiolet JW, Wilms-Schopman FJ, Schaapherder AF, Johnson TA, Gettes LS, Janse MJ, “Distribution of extracellular potassium and its relation to electrophysiologic changes during acute myocardial ischemia in the isolated perfused porcine heart”, Circulation. 1988 May;77(5):1125-38.
- Ferrero (Jr) JM; Trénor B; Rodríguez B; Sáiz J, “Electrical Activity and Reentry During Acute Regional Myocardial Ischemia: Insights from Simulations”, International Journal of Bifurcation and Chaos 2003; 13(12):3703-3715.
- Heidenreich EA, Ferrero JM, Doblaré M, Rodríguez JF, “Adaptive Macro Finite Elements for the Numerical Solution of Monodomain Equations in Cardiac Electrophysiology”, Annals of Biomedical Engineering 2010; 38(7):2331-2345.
- Heidenreich EA, Gaspar FJ, Ferrero JM, J. F. Rodríguez, “Compact schemes for anisotropic reaction-diffusion equations with adaptive time step”, International Journal for Numerical Methods in Engineering 2010; 82(8):1022-1043.
- Trénor B, Romero L, Ferrero JM Jr, Sáiz J, Moltó G, Alonso JM, “Vulnerability to reentry in a regionally ischemic tissue: a simulation study”, Ann Biomed Eng. 2007 Oct;35(10):1756-70.
- Romero L, Trénor B, Alonso JM, Tobón C, Saiz J, Ferrero JM Jr, “The relative role of refractoriness and source-sink relationship in reentry generation during simulated acute ischemia”, Ann Biomed Eng. 2009 Aug;37(8):1560-71.