

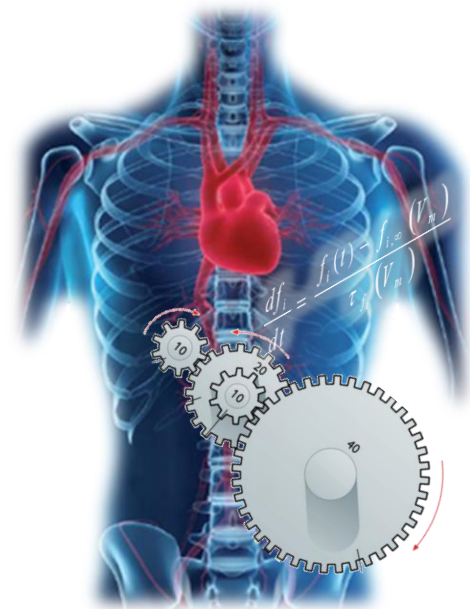
TEMA 11

MODELADO Y SIMULACIÓN DE LA ACTIVIDAD BIOELÉCTRICA DEL CORAZÓN

Chema Ferrero

Bioelectricidad

Grado en Ingeniería Biomédica



Esquema de exposición

BASE TEÓRICA: Modelos computacionales de la actividad bioeléctrica del corazón

Descripción de la isquemia aguda y el infarto

INVESTIGACIÓN: Análisis de los mecanismos arritmogénicos de la isquemia miocárdica

DESARROLLO: Simulación personalizada de ablación por RF en pacientes con infarto de miocardio



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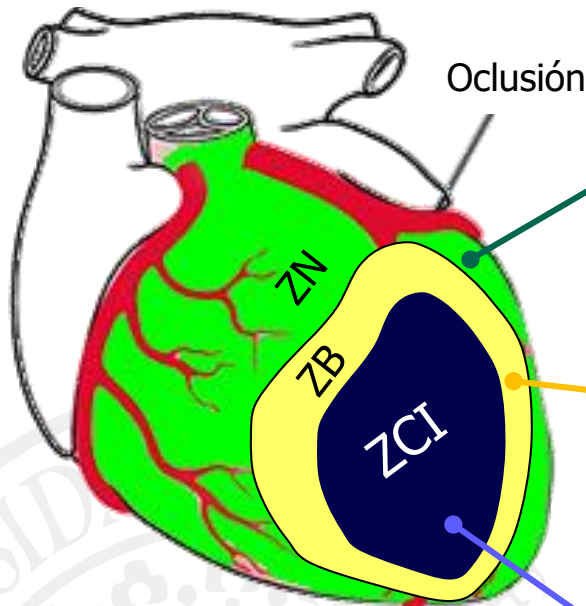
DESARROLLO: Simulación personalizada de ablación por RF en pacientes con infarto de miocardio



Isquemia aguda e infarto de miocardio

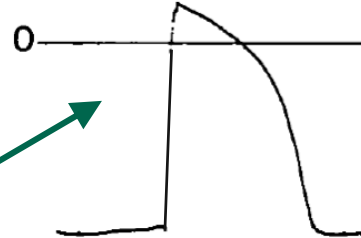
0-30 min: ISQUEMIA AGUDA

30 min →: INFARTO

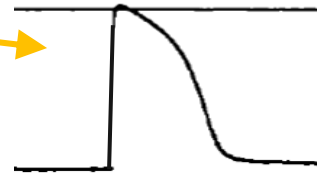


ZCI: Zona Central Isquémica
ZB: Zona de Borde
ZN: Zona Normal

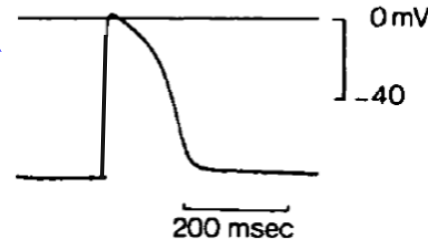
Zona Normal



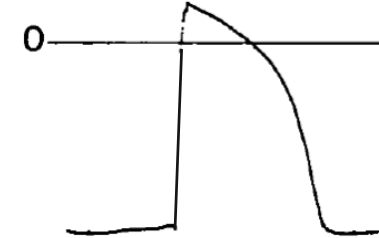
Zona de Borde



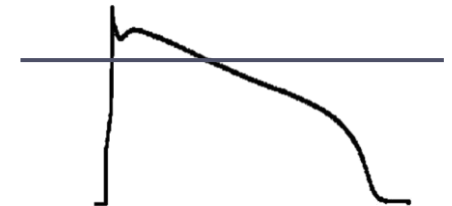
Zona Central Isquémica



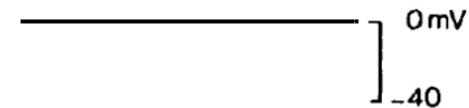
Zona Normal



Zona de Borde



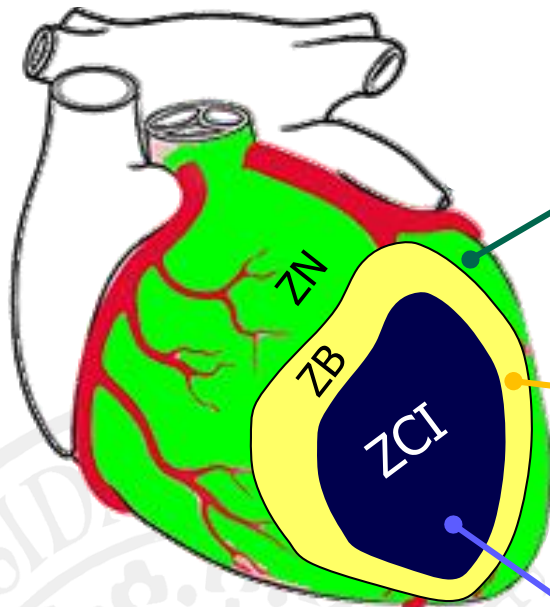
Cicatriz del Infarto



Isquemia aguda e infarto de miocardio

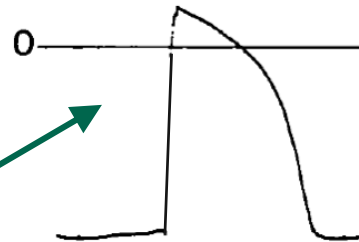
0-30 min: ISQUEMIA AGUDA

30 min →: INFARTO

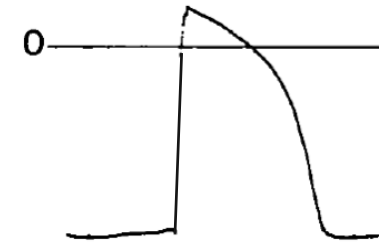


ZCI: Zona Central Isquémica
ZB: Zona de Borde
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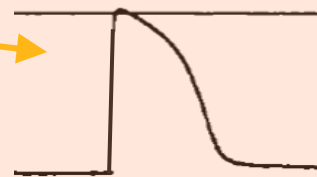
Zona Normal



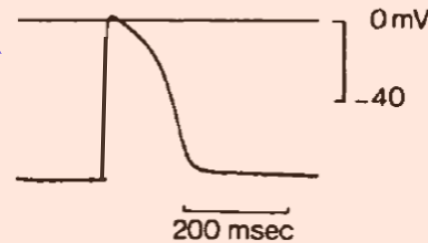
Zona Normal



Zona de Borde

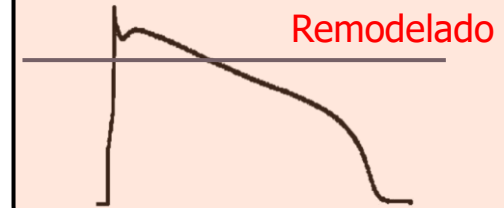


Zona Central Isquémica



Efecto directo de los cambios metabólicos

Zona de Borde



Cicatriz del Infarto

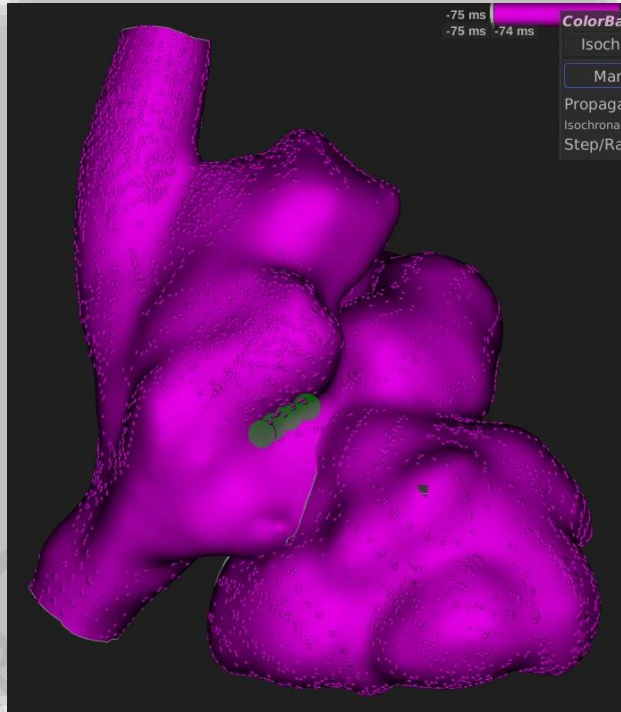


Muerte celular

Isquemia aguda e infarto de miocardio

(tiempo ÷ 25)

[Ferrero et al, 2018]



Ritmo Sinusal



0-30 min: ISQUEMIA AGUDA

[Gray et al., 1995]

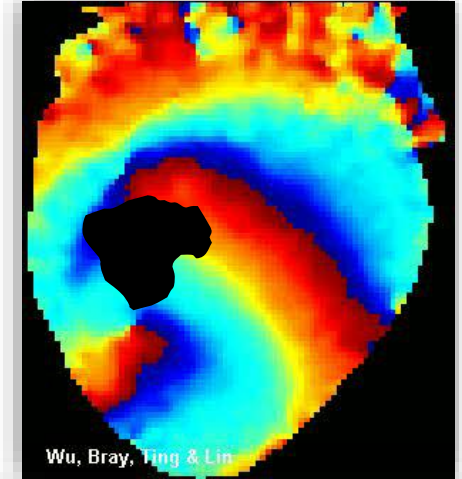


Fibrilación Ventricular



30 min →: INFARTO

[Wu et al, 2006]

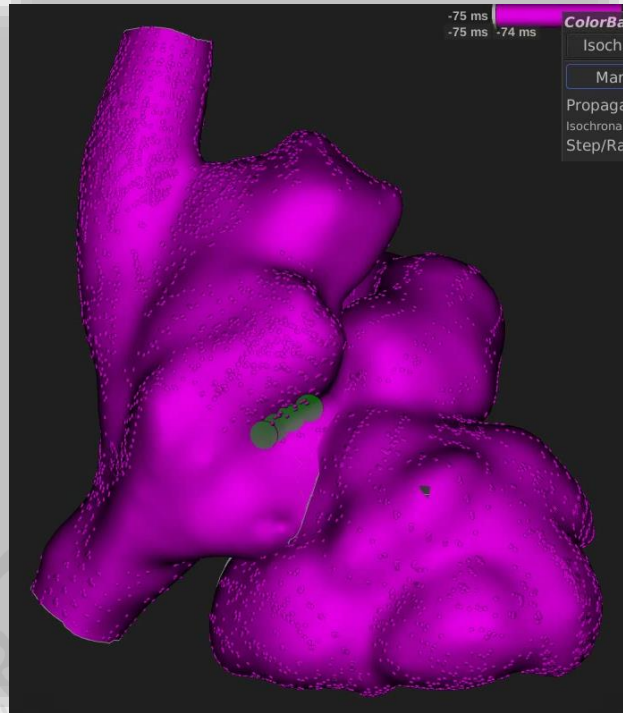


Taquicardia Ventricular



Isquemia aguda e infarto de miocardio

[Ferrero et al, 2018]



Ritmo Sinusal



0-30 min: ISQUEMIA AGUDA

[Gray et al., 1995]



Fibrilación Ventricular

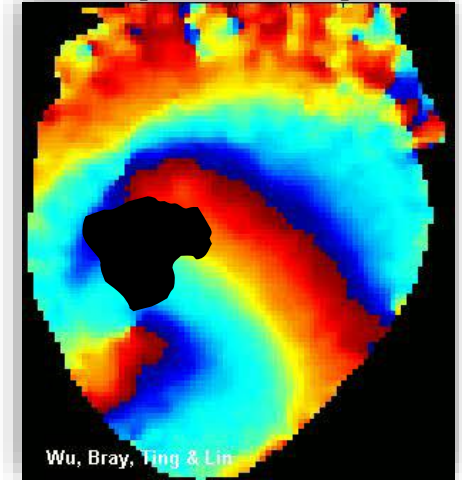


7,000,000 de muertes al año en todo el mundo

RIESGO DE SUFRIR ARRITMIAS

30 min →: INFARTO

[Wu et al, 2006]



Taquicardia Ventricular

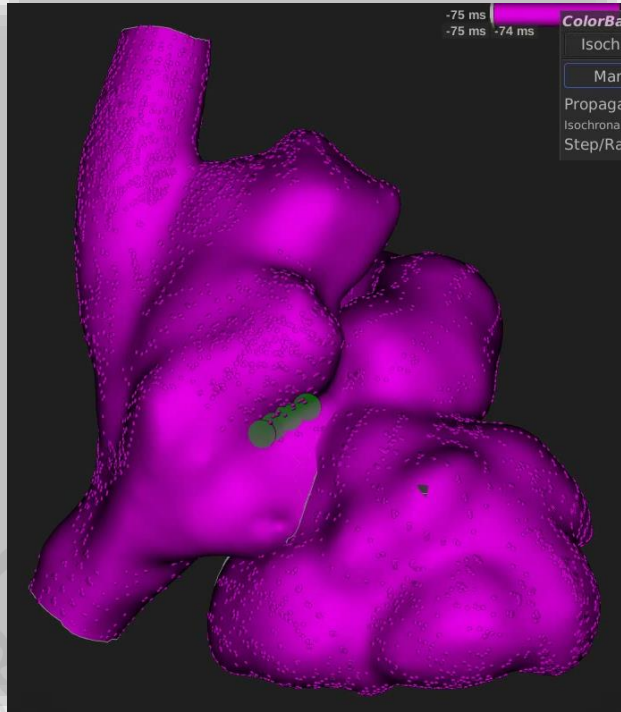
//

horas, días, meses, años...

[Smith et al,1995]

Isquemia aguda e infarto de miocardio

[Ferrero et al, 2018]



Ritmo Sinusal

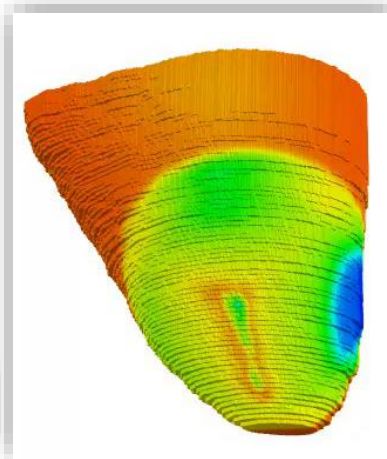


0-30 min: ISQUEMIA AGUDA

[Gray et al., 1995]



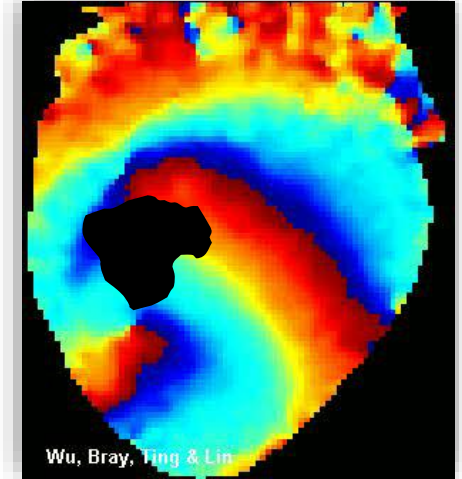
Fibrilación Ventricular



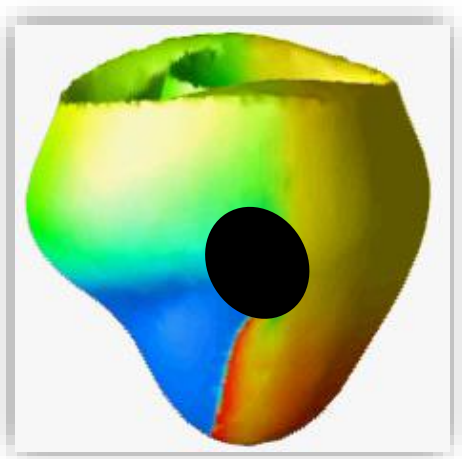
[Rodríguez & Ferrero, 2015]

30 min →: INFARTO

[Wu et al, 2006]



Taquicardia Ventricular



[Trayanova et al, 2006]

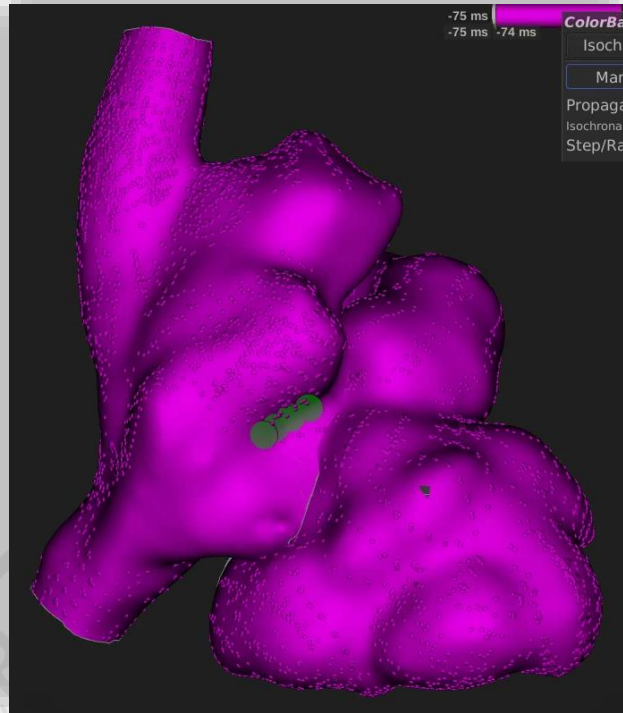
EXPERIMENTOS

SIMULACIONES

Isquemia aguda e infarto de miocardio

0-30 min: ISQUEMIA AGUDA

[Ferrero et al, 2018]



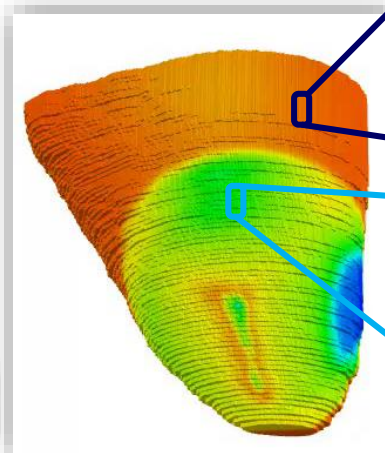
Ritmo Sinusal



[Gray et al., 1995]

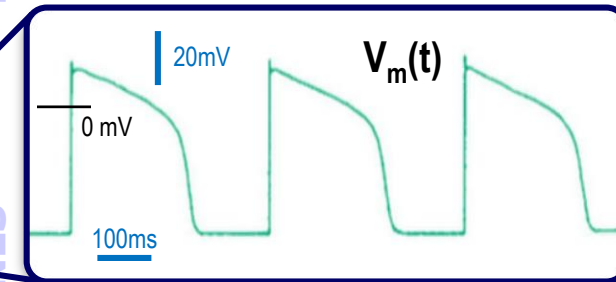


Fibrilación Ventricular

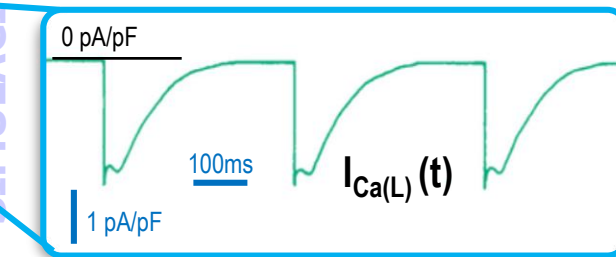


[Rodríguez & Ferrero, 2015]

EXPERIMENTOS



SIMULACIONES

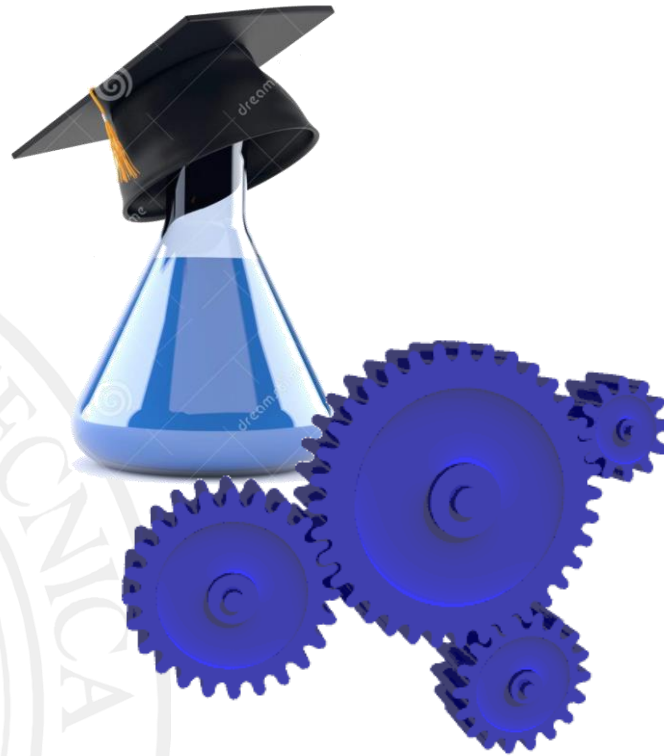


Esquema de exposición

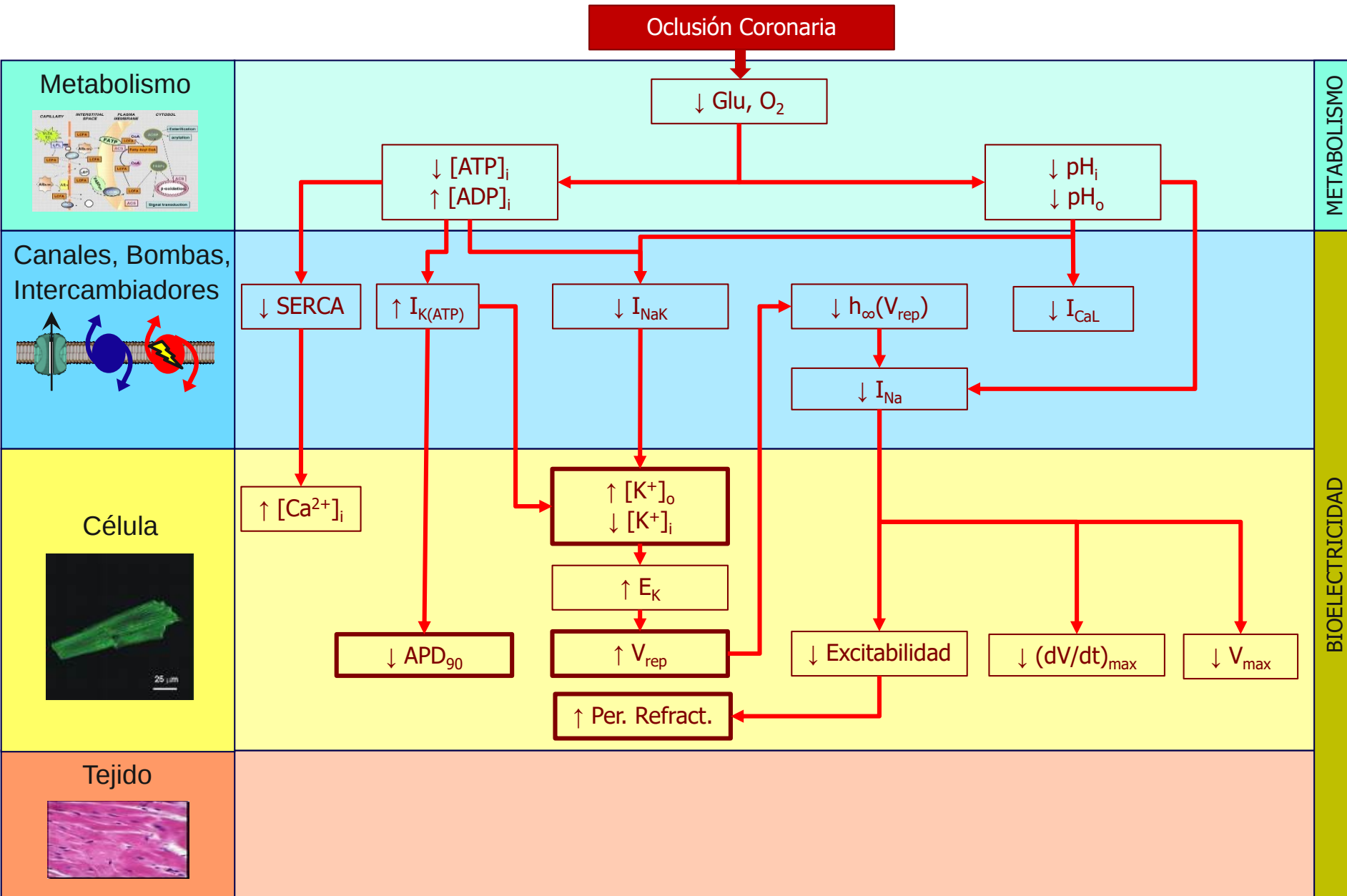
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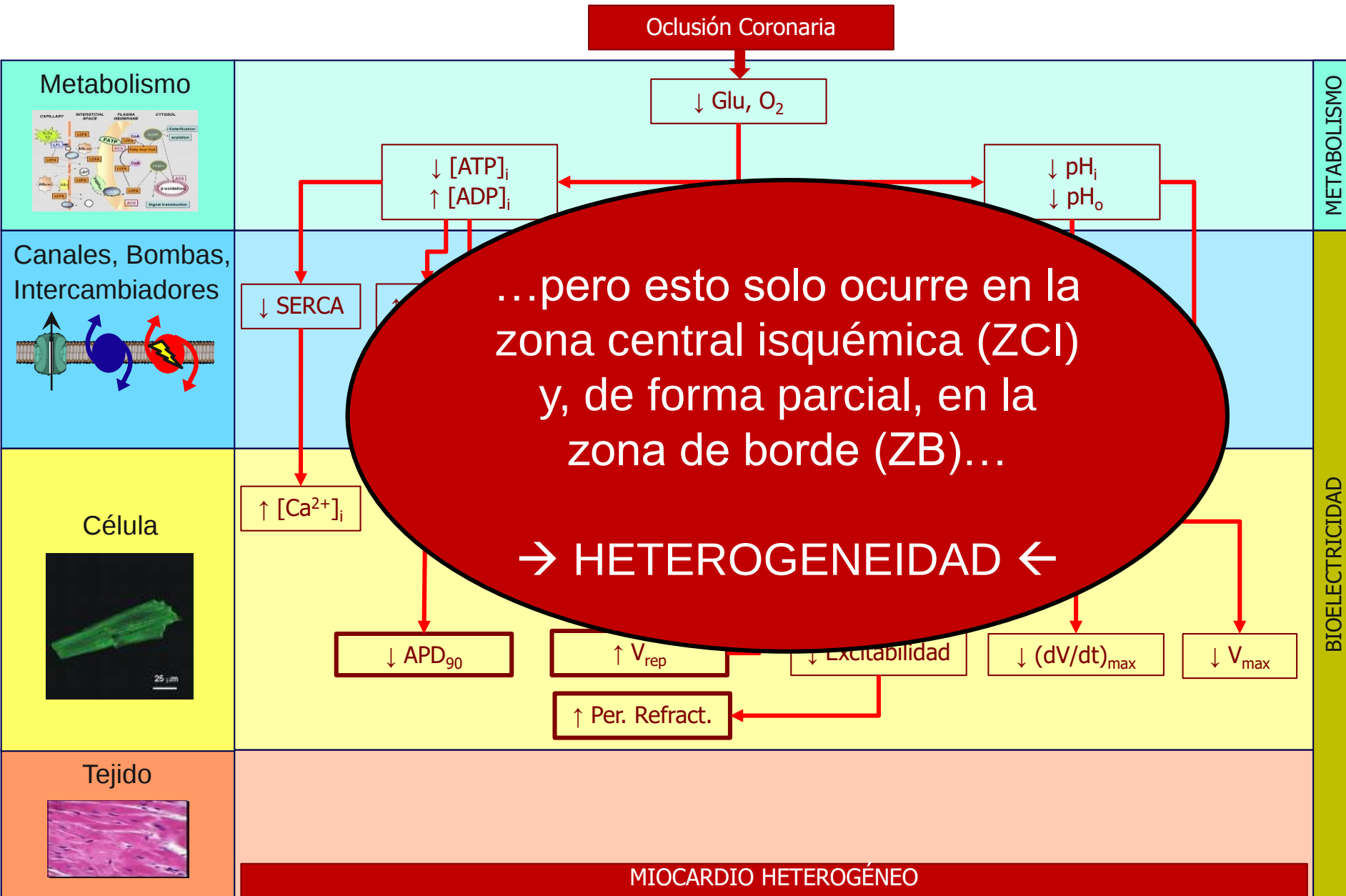
DESARROLLO: Simulación personalizada de ablación por RF en pacientes con infarto de miocardio

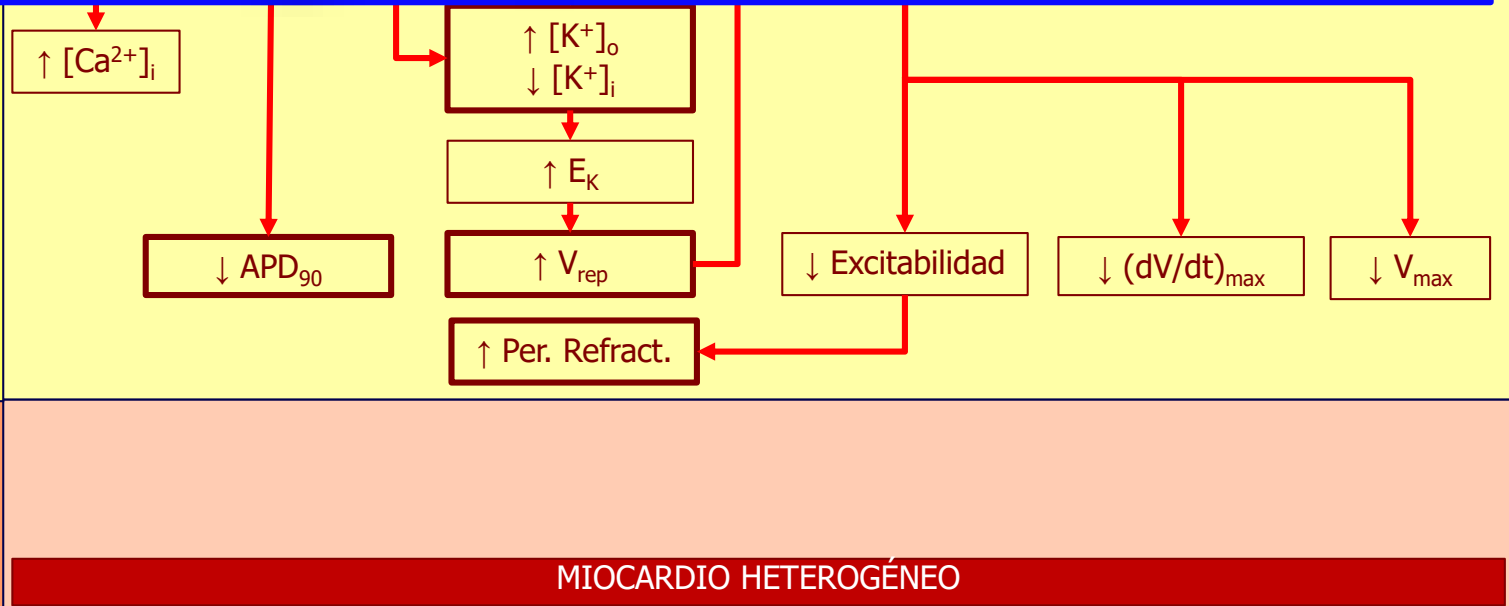
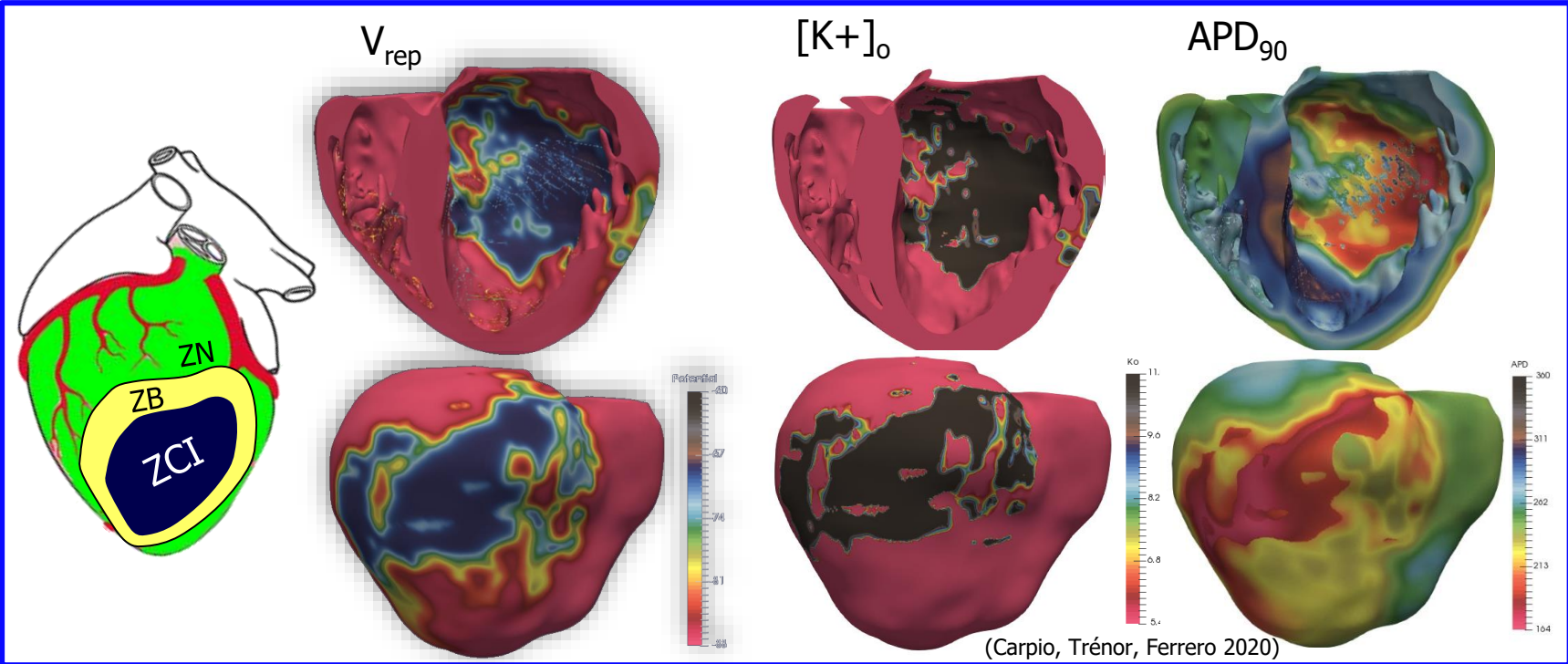


Efectos de la isquemia miocárdica aguda sobre la bioelectricidad cardiaca

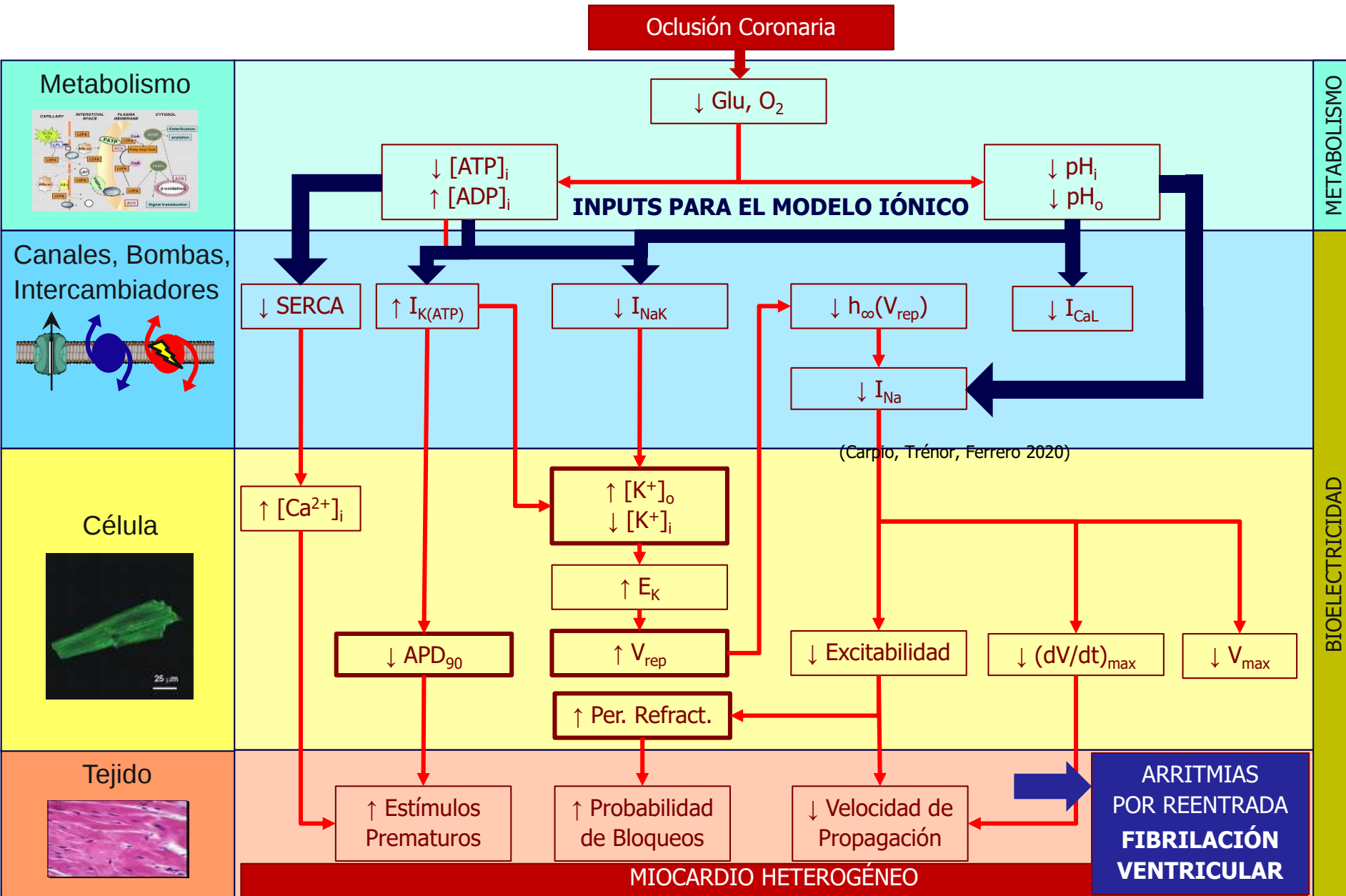


Efectos de la isquemia miocárdica aguda sobre la bioelectricidad cardiaca





Efectos de la isquemia miocárdica aguda sobre la bioelectricidad cardiaca



Modelado multiescala de la isquemia miocárdica

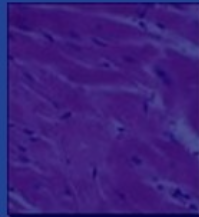
Cuerpo



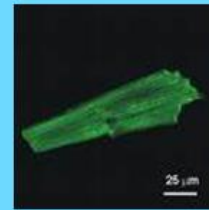
Órgano



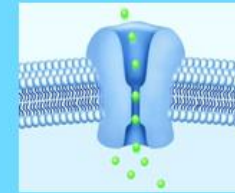
Tejido



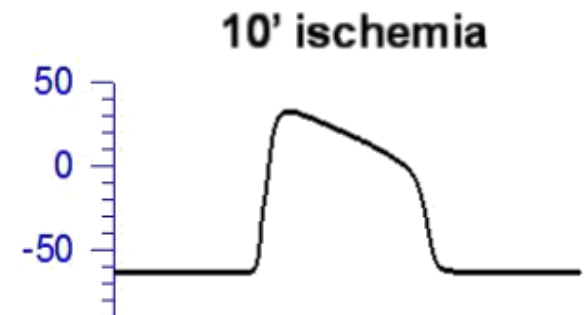
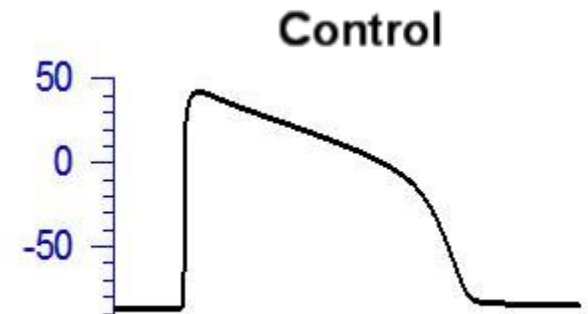
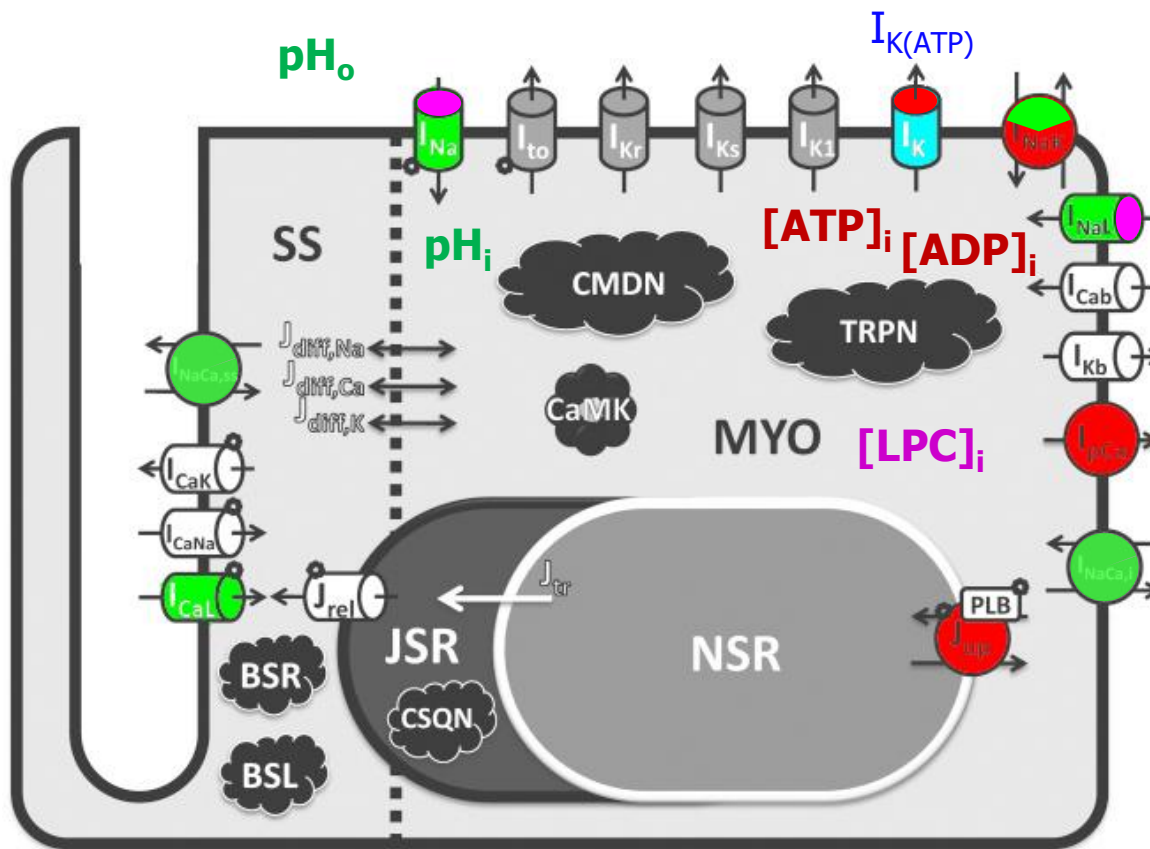
Célula



Canal Iónico



Gen



Modelado multiescala de la isquemia miocárdica

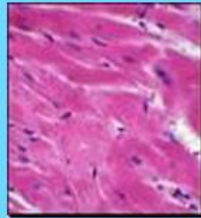
Cuerpo



Órgano



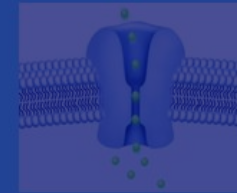
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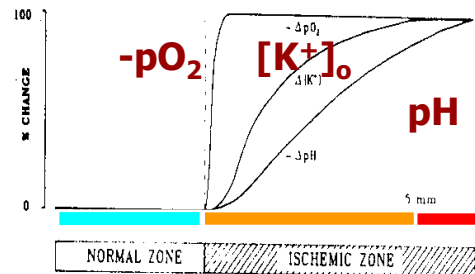
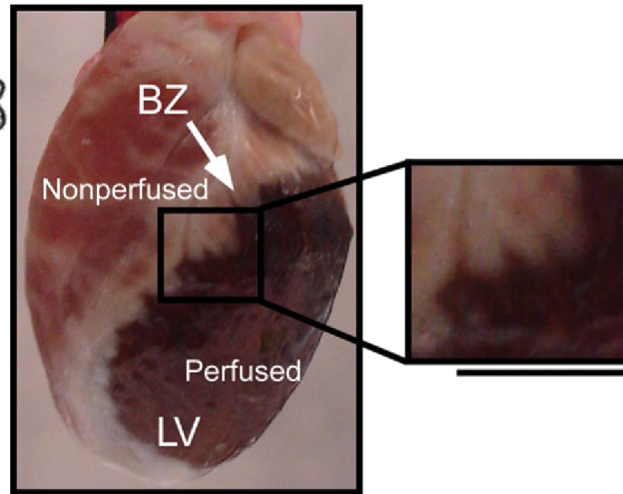
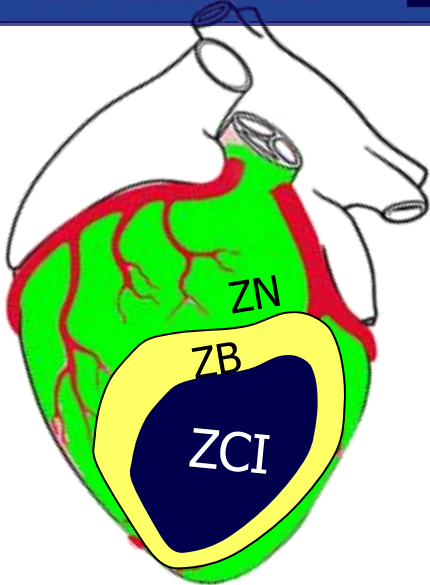
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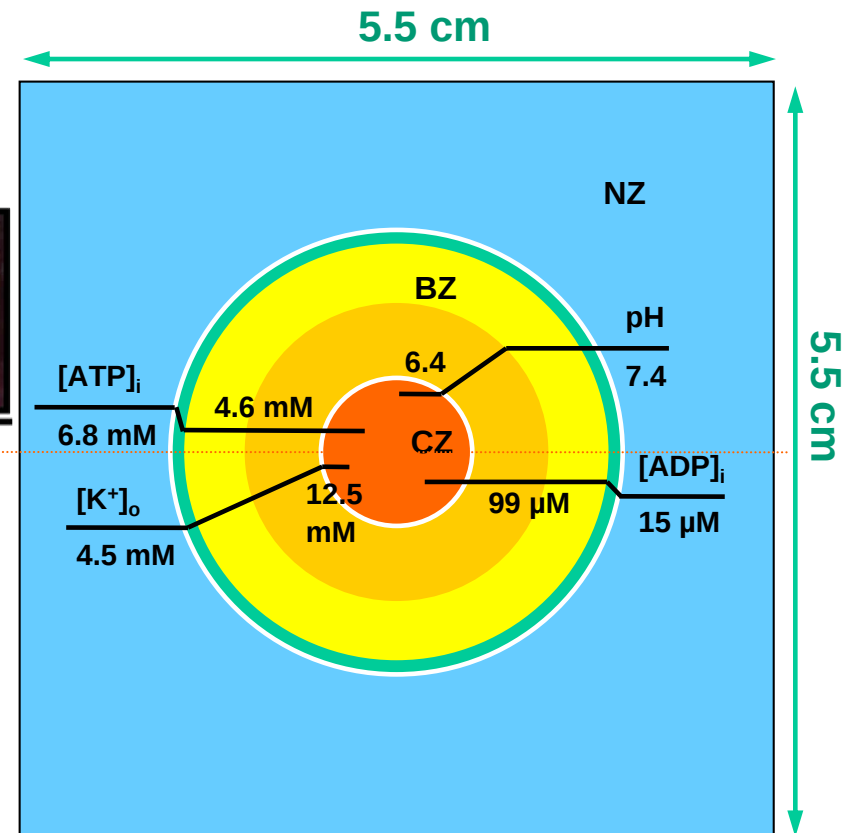
Canal Iónico



Gen



[Coronel et al, Circ Res 1988]



[Ferrero et al, Int J Bifurcation & Chaos, 2003]

Modelado multiescala de la isquemia miocárdica

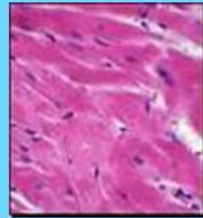
Cuerpo



Órgano



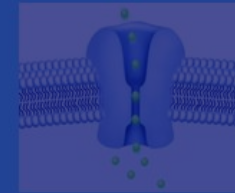
Tejido



Célula



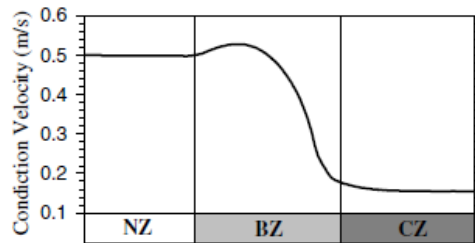
Canal Iónico



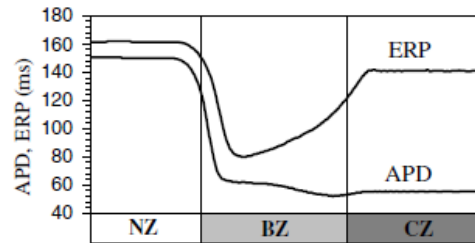
Gen



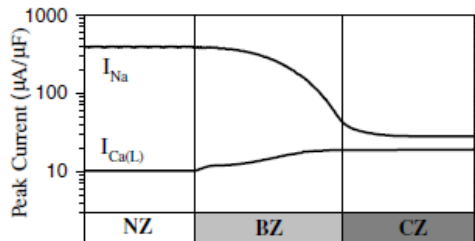
(a)



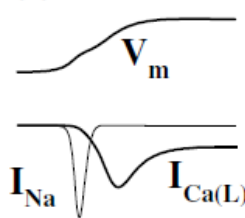
(b)



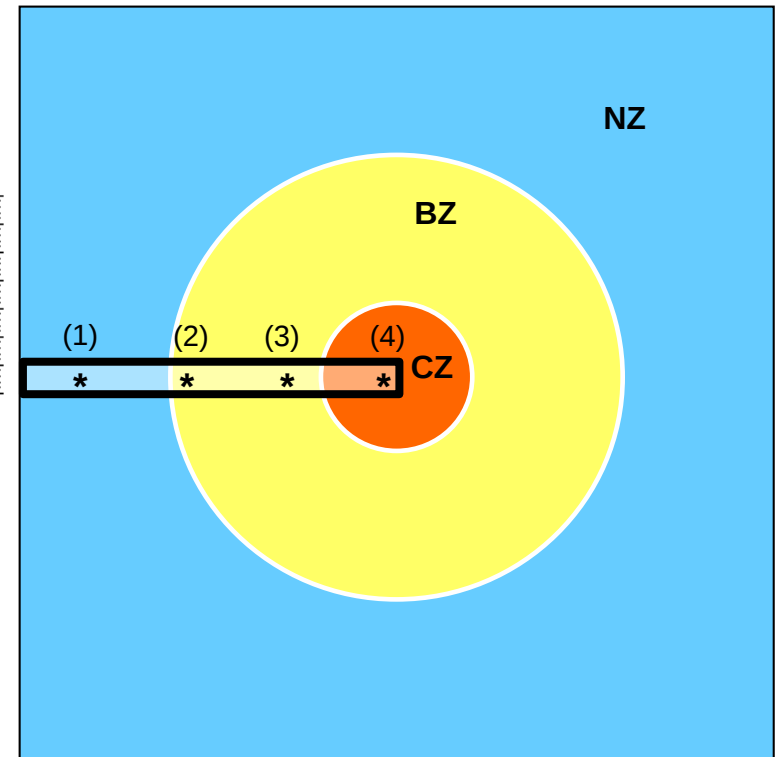
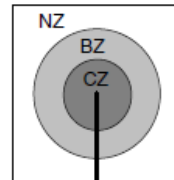
(c)



(d)



(e)



[Ferrero et al, *Int J Bifurcation & Chaos*, 2003]

Modelado multiescala de la isquemia miocárdica

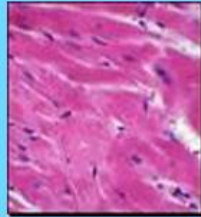
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Órgano



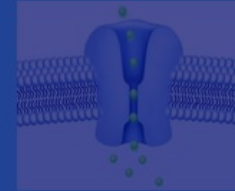
Tejido



Célula



Canal Iónico



Gen

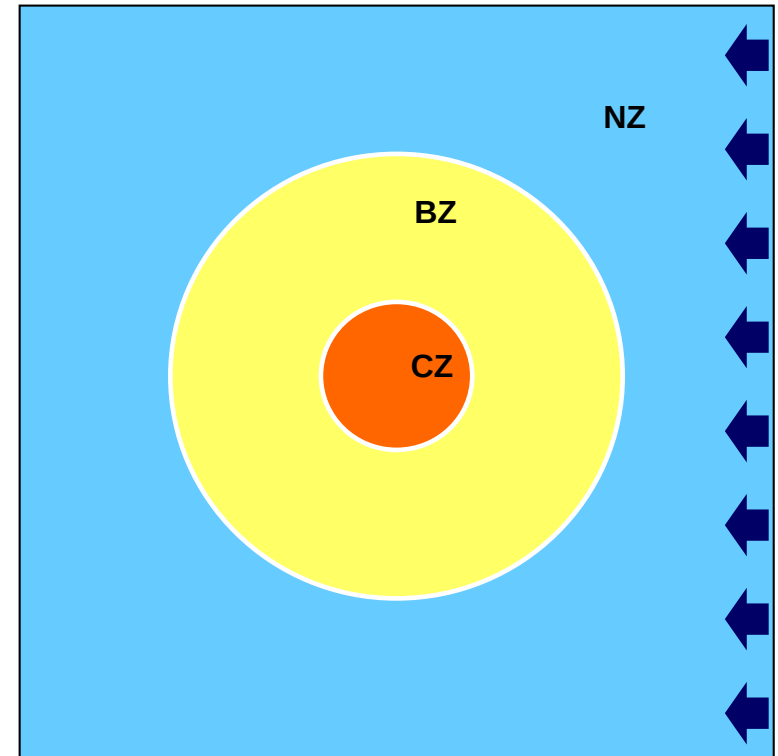


S1

S1

S2

CI variable



[Ferrero et al, *Int J Bifurcation & Chaos*, 2003]

Modelado multiescala de la isquemia miocárdica

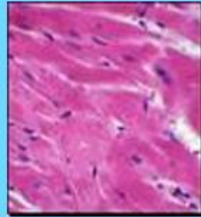
Cuerpo



Órgano



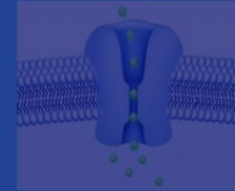
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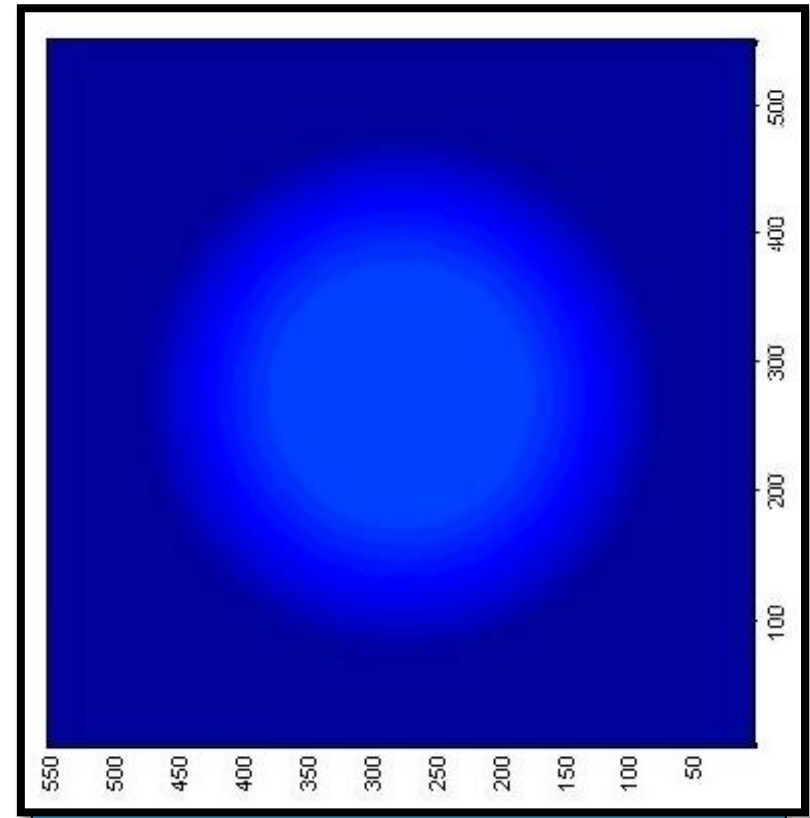
Célula



Canal Iónico



Gen



[Ferrero et al, *Int J Bifurcation & Chaos*, 2003]

Modelado multiescala de la isquemia miocárdica

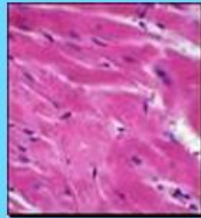
Cuerpo



Órgano



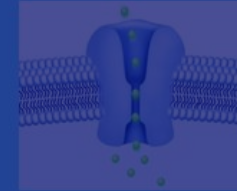
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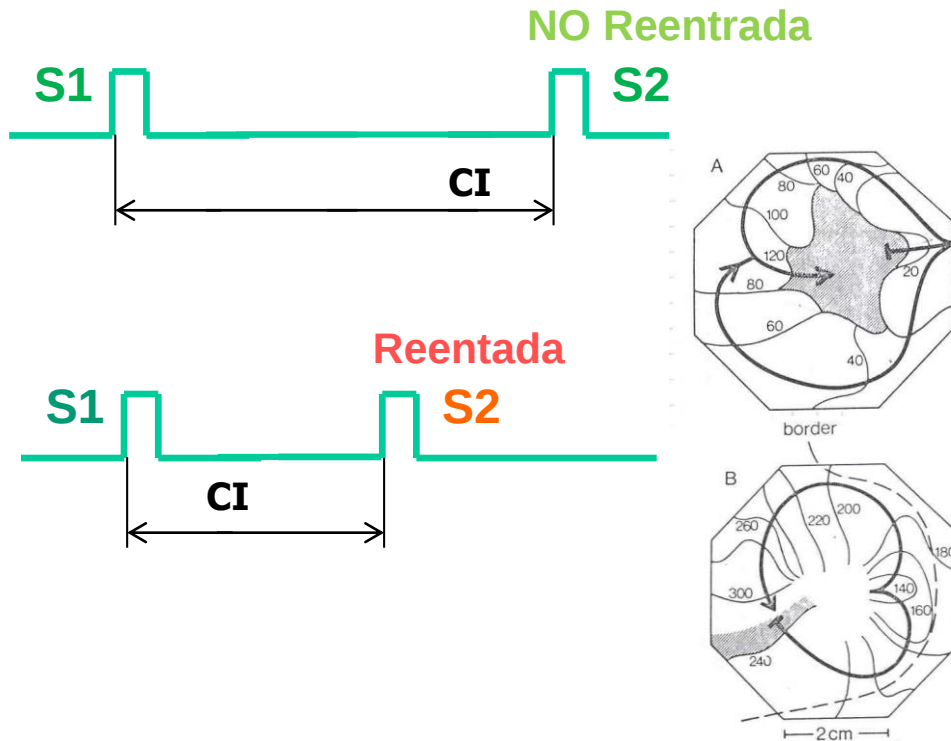
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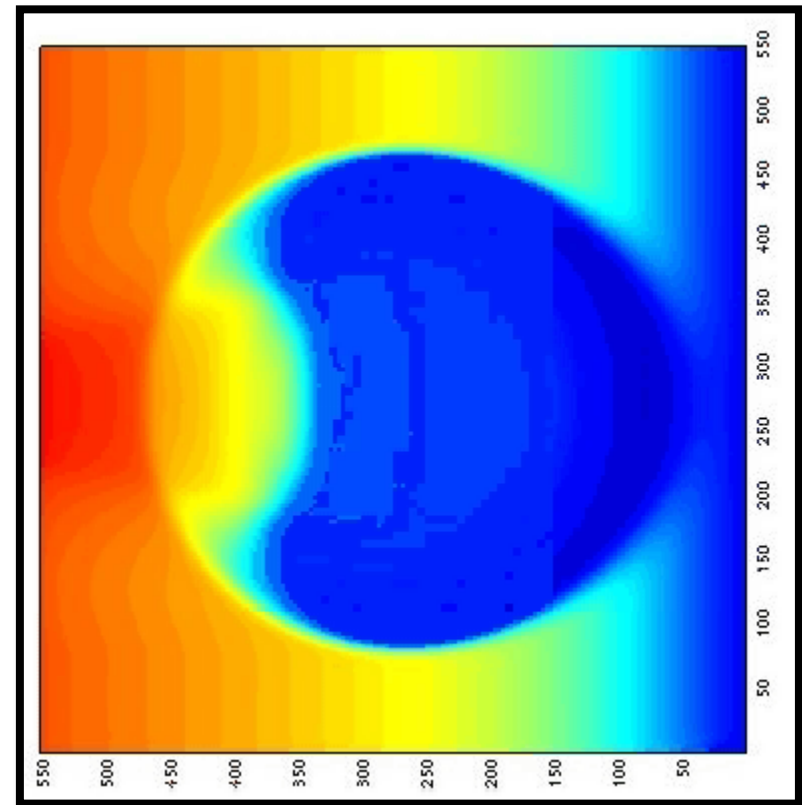
Canal Iónico



Gen



[Janse et al, *Circ Res*, 1981]



[Ferrero et al, *Int J Bifurcation & Chaos*, 2003]

Modelado multiescala de la isquemia miocárdica

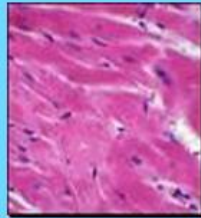
Cuerpo



Órgano



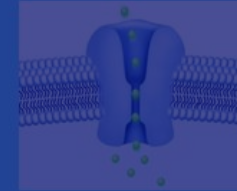
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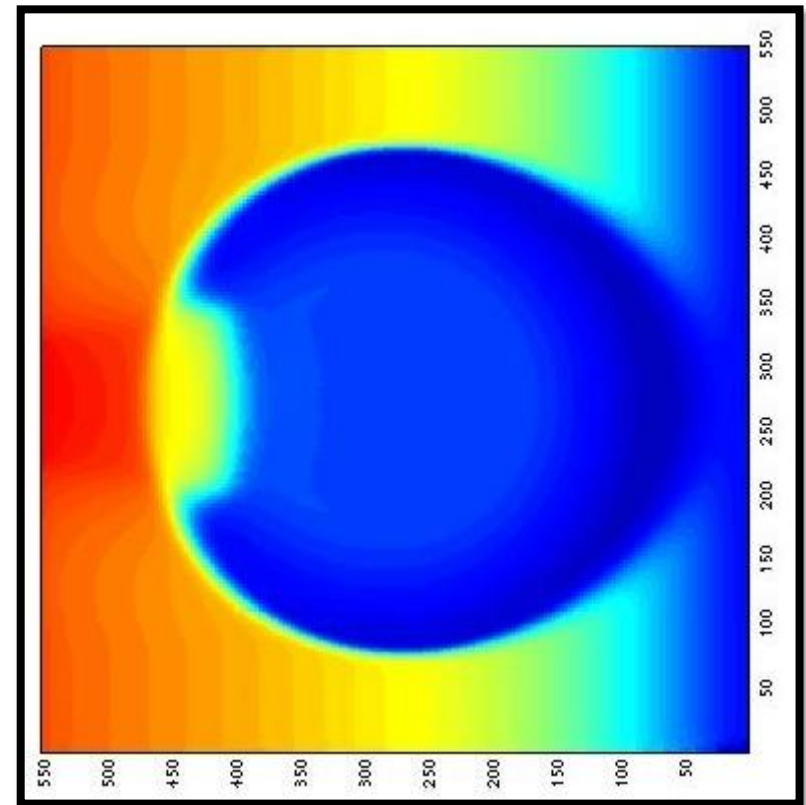
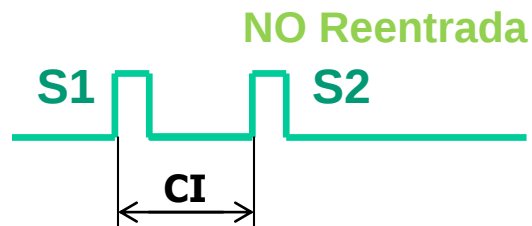
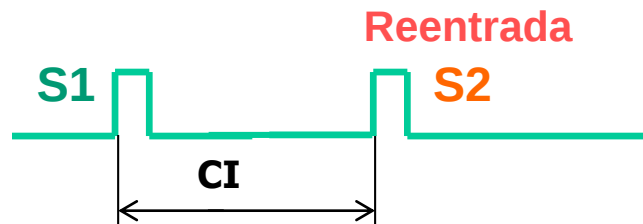
Célula



Canal Iónico



Gen



[Ferrero et al, *Int J Bifurcation & Chaos*, 2003]

Modelado multiescala de la isquemia miocárdica

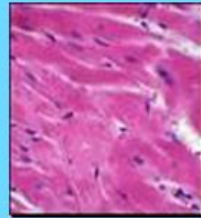
Cuerpo



Órgano



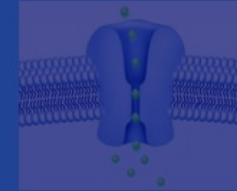
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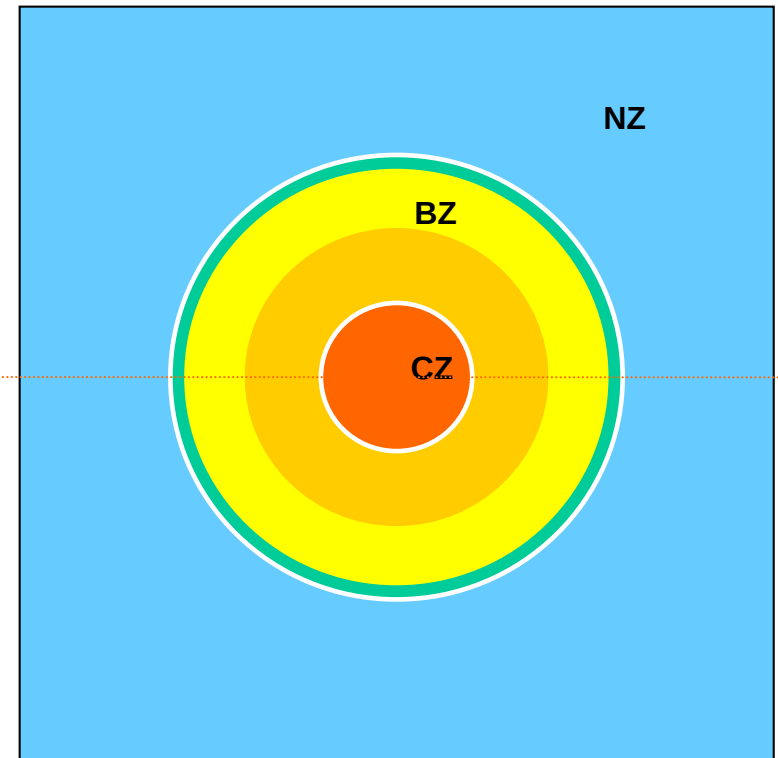
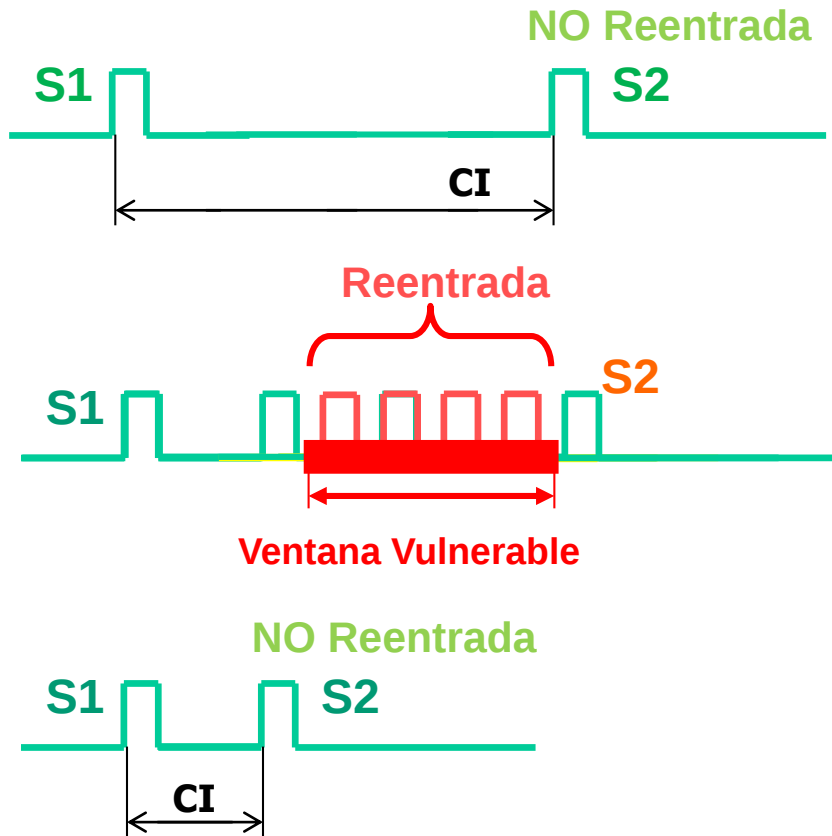
Célula



Canal Iónico



Gen



[Ferrero et al, *Int J Bifurcation & Chaos*, 2003]

Modelado multiescala de la isquemia miocárdica

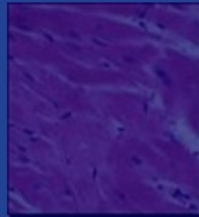
Cuerpo



Órgano



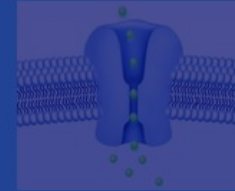
Tejido



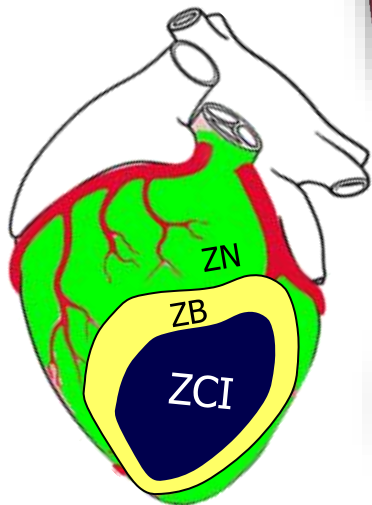
Célula



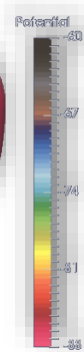
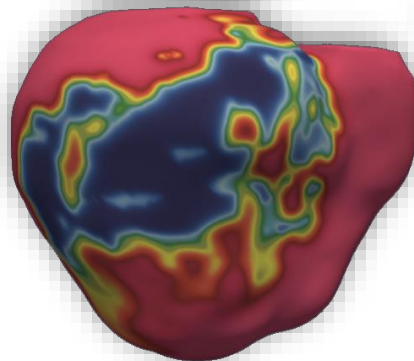
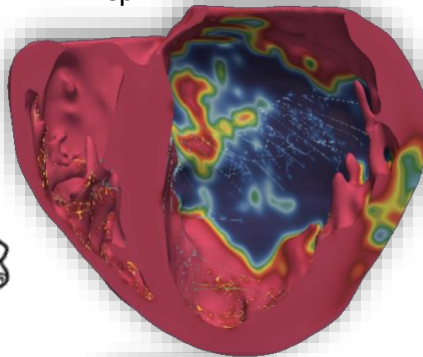
Canal Iónico



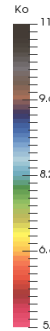
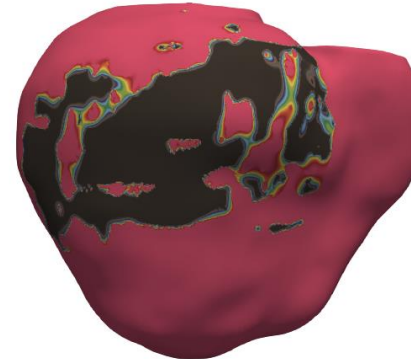
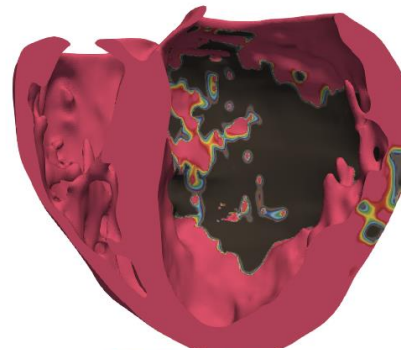
Gen



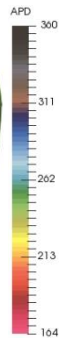
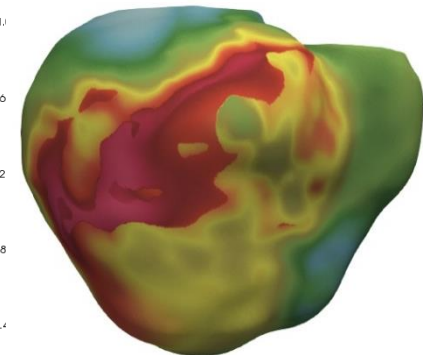
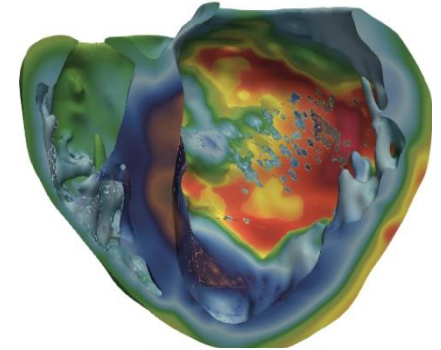
V_{rep}



$[K^+]_o$



APD_{90}



[Carpio, Trénor & Ferrero, 2020]

Modelado multiescala de la isquemia miocárdica

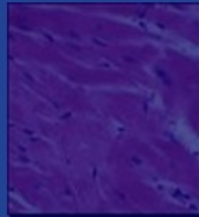
Cuerpo



Órgano



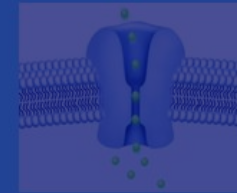
Tejido



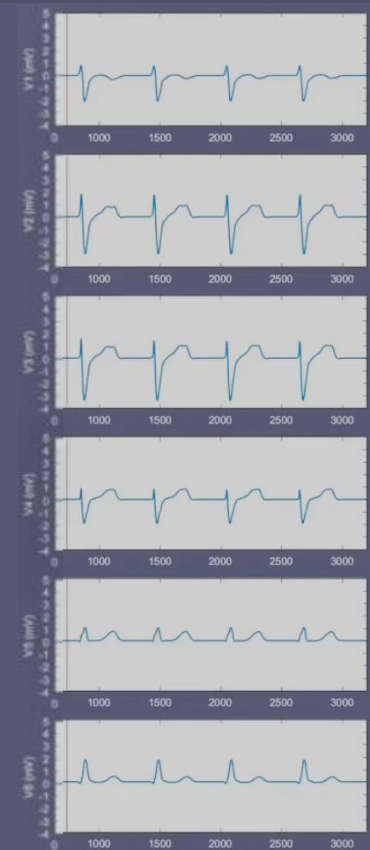
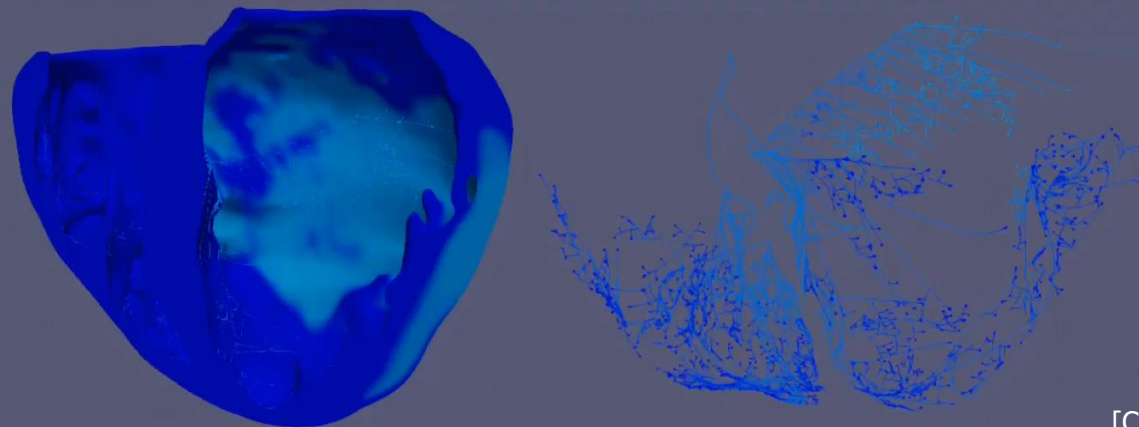
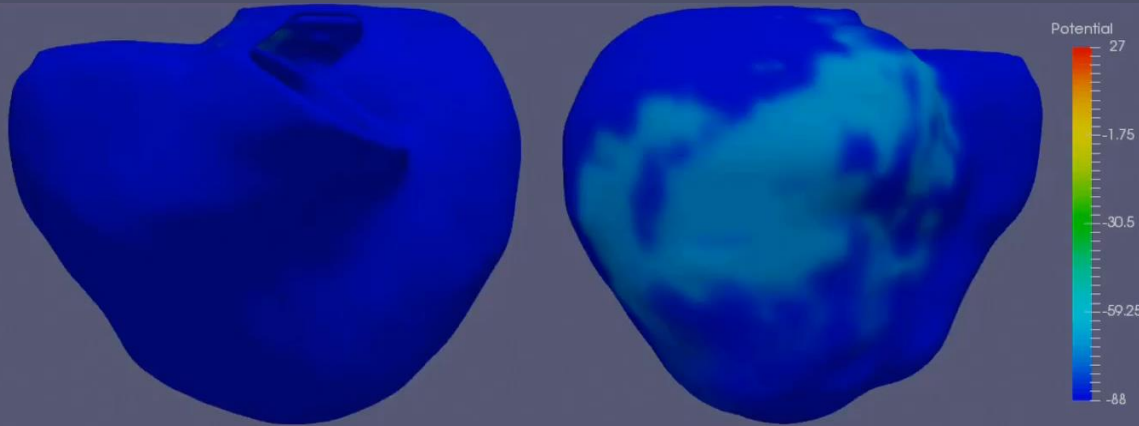
Célula



Canal Iónico



Gen



[Carpio, Trénor & Ferrero, 2020]

Modelado multiescala de la isquemia miocárdica

Cuerpo



Órgano



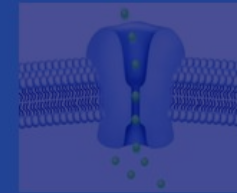
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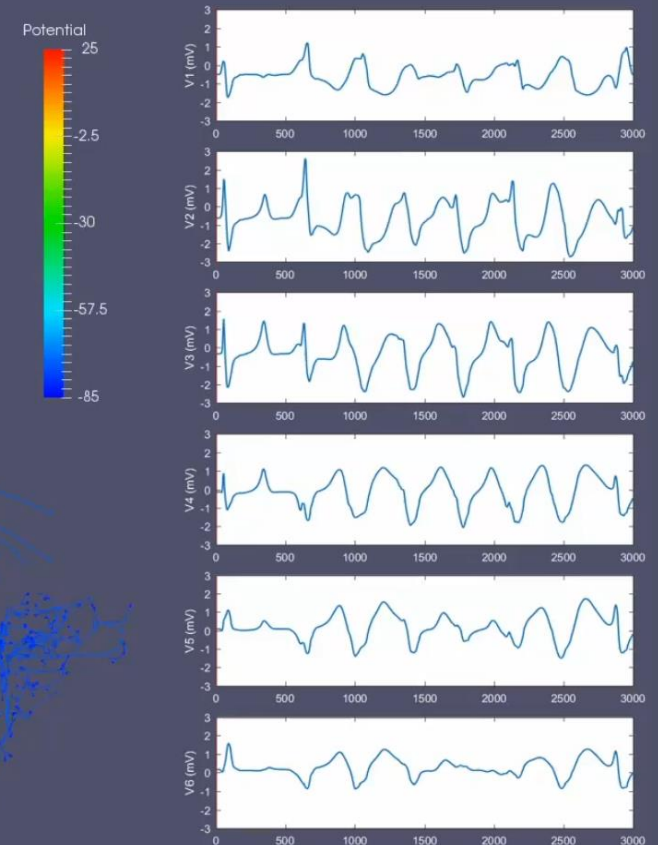
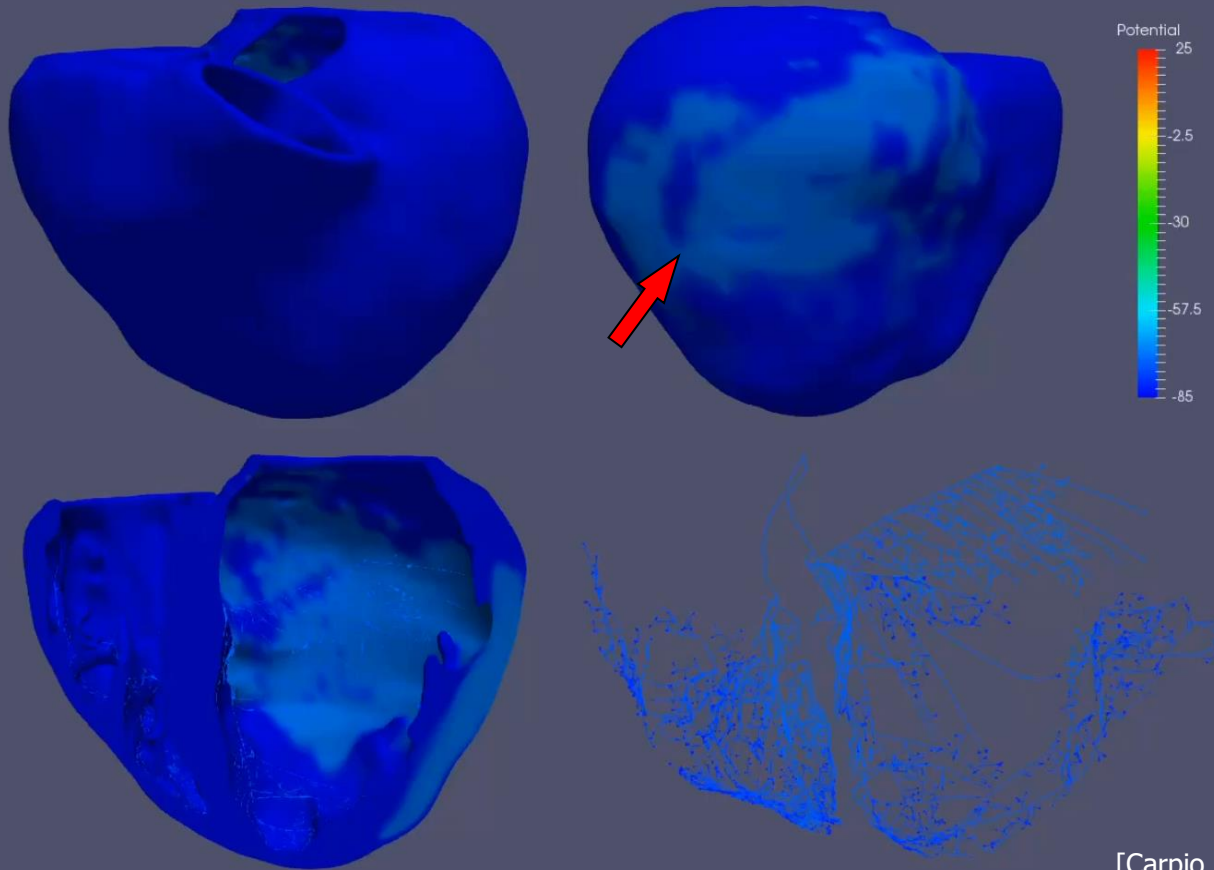
Célula



Canal Iónico



Gen



[Carpio, Trénor & Ferrero, 2020] (ms)

Modelado multiescala de la isquemia miocárdica

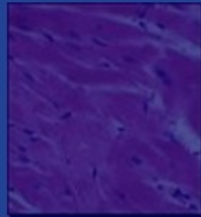
Cuerpo



Órgano



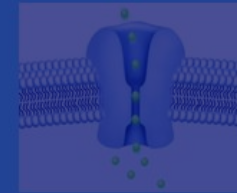
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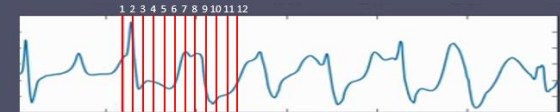
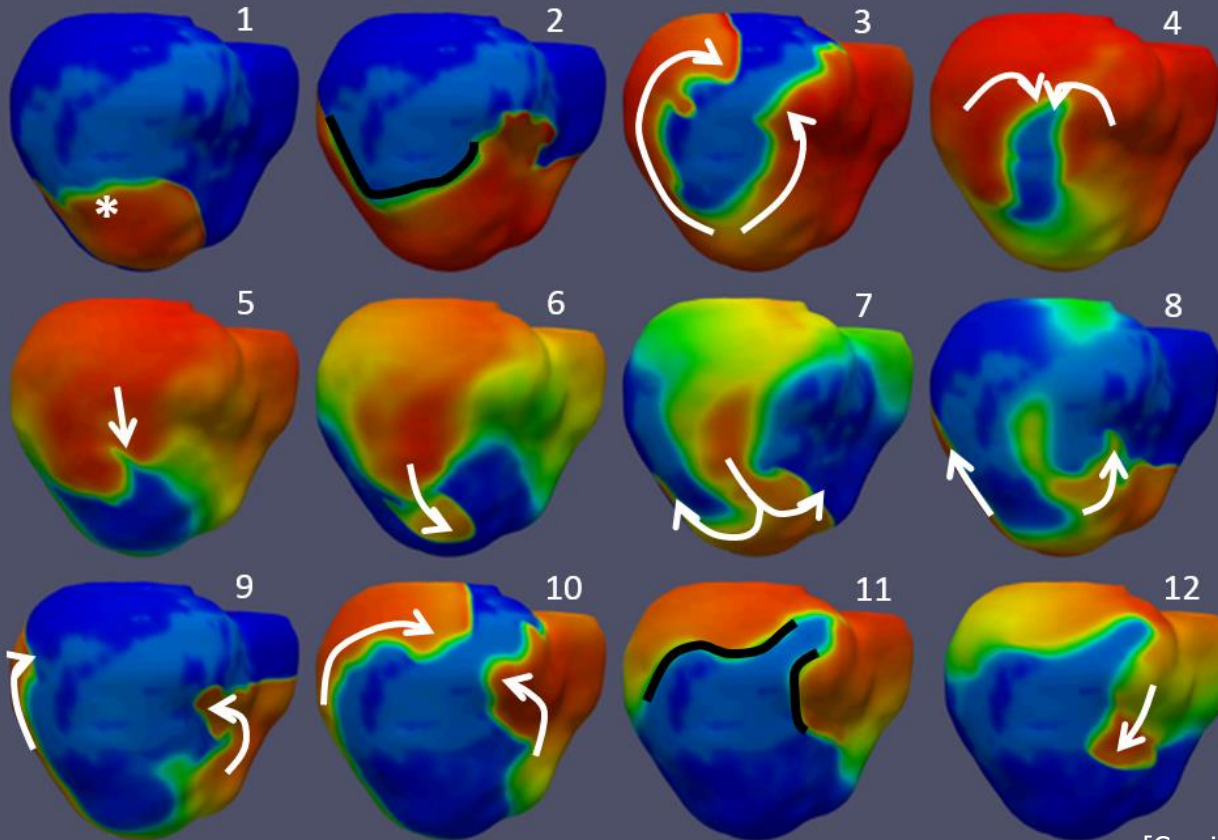
Célula



Canal Iónico



Gen



[Carpio, Trénor & Ferrero, 2020]

Modelado multiescala de la isquemia miocárdica

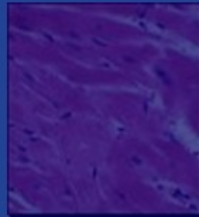
Cuerpo



Órgano



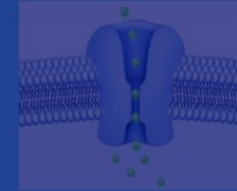
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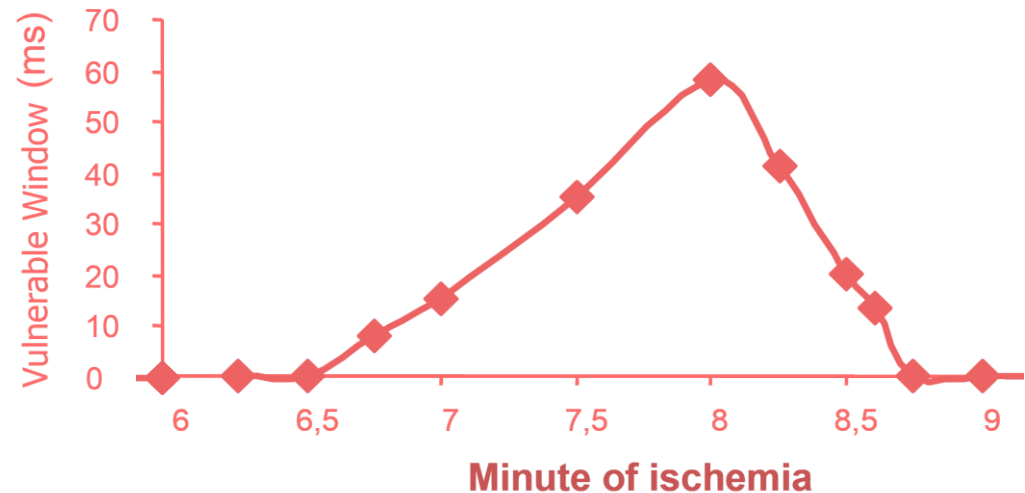
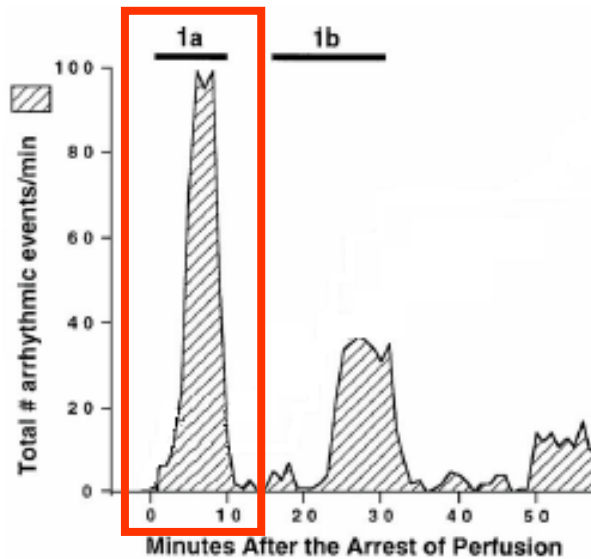
Célula



Canal Iónico



Gen



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

Romero, Trenor & Ferrero, Ann Biomed Eng 2009

Modelado multiescala de la isquemia miocárdica

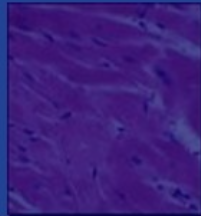
Cuerpo



Órgano



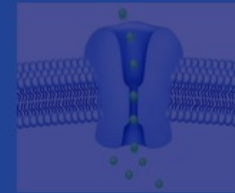
Tejido



Célula



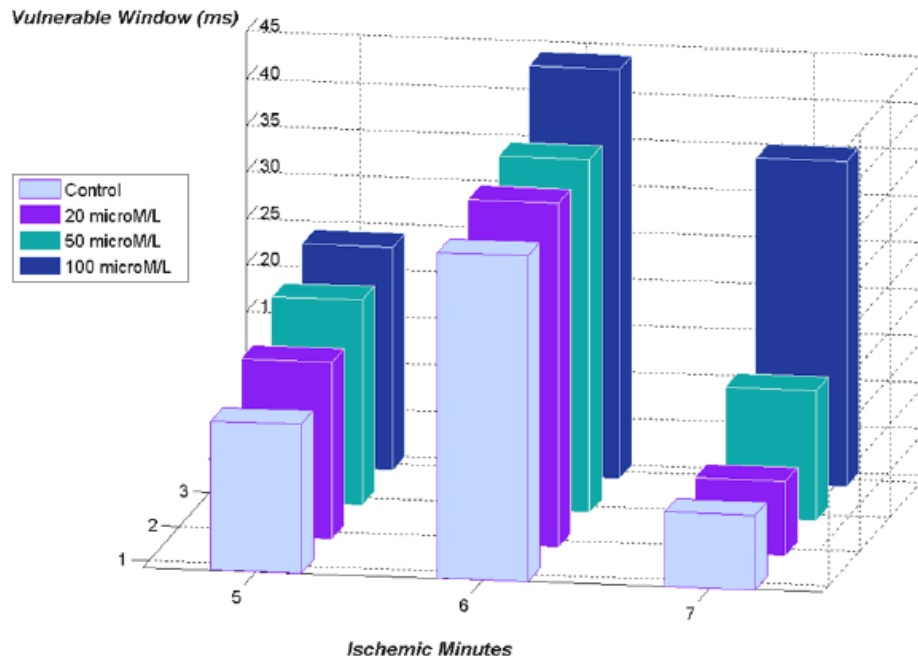
Canal Iónico



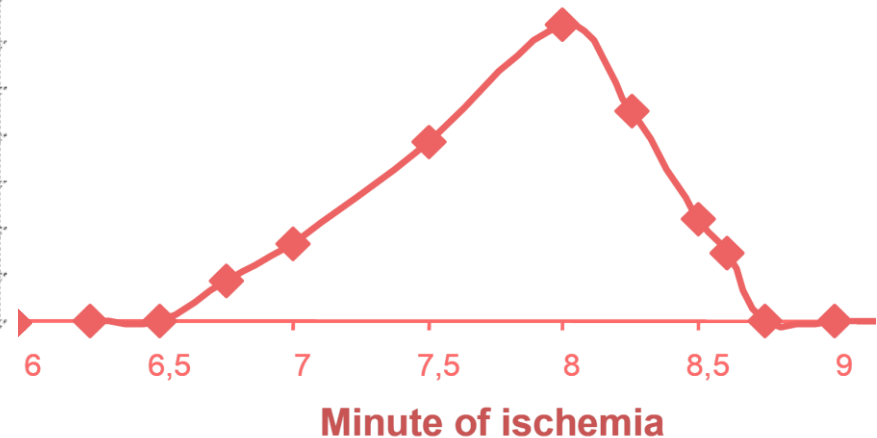
Gen



Lidocaine modulates the VW in ischemia



Cardona, Ferrero & Saiz Am J Physiol 2010



Romero, Trenor & Ferrero, Ann Biomed Eng 2009

Modelado multiescala de la isquemia miocárdica

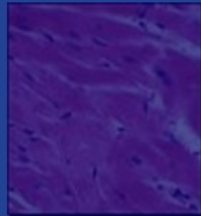
Cuerpo



Órgano



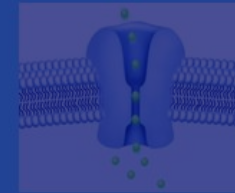
Tejido



Célula



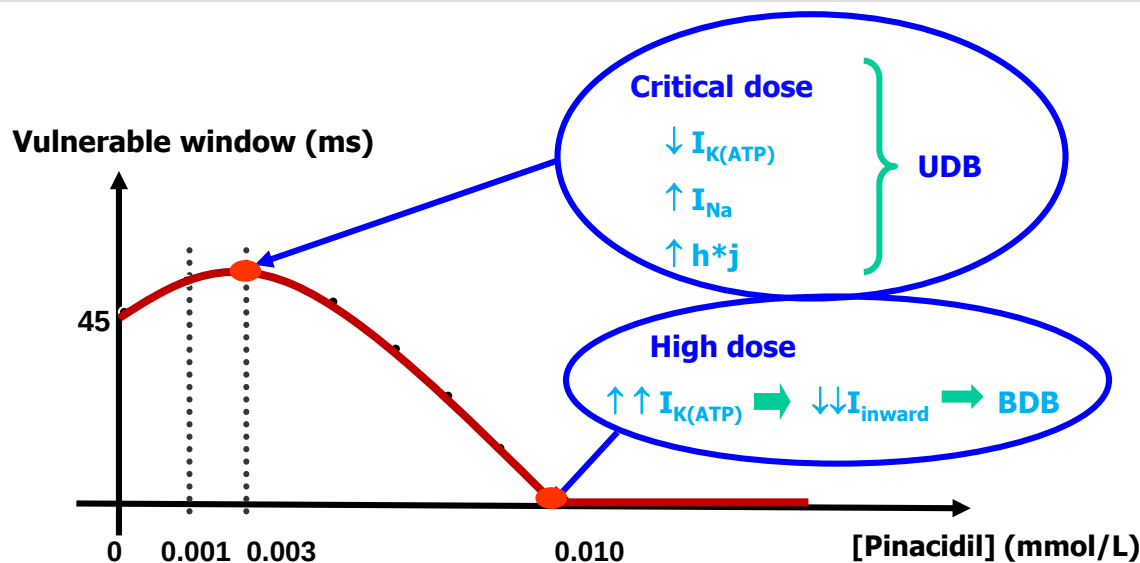
Canal Iónico



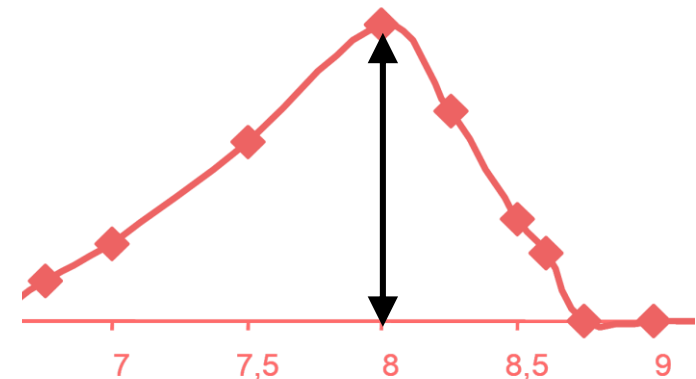
Gen



Pinacidil modulates the VW in ischemia



Trenor, Rodríguez & Ferrero, Ann Biomed Eng 2009



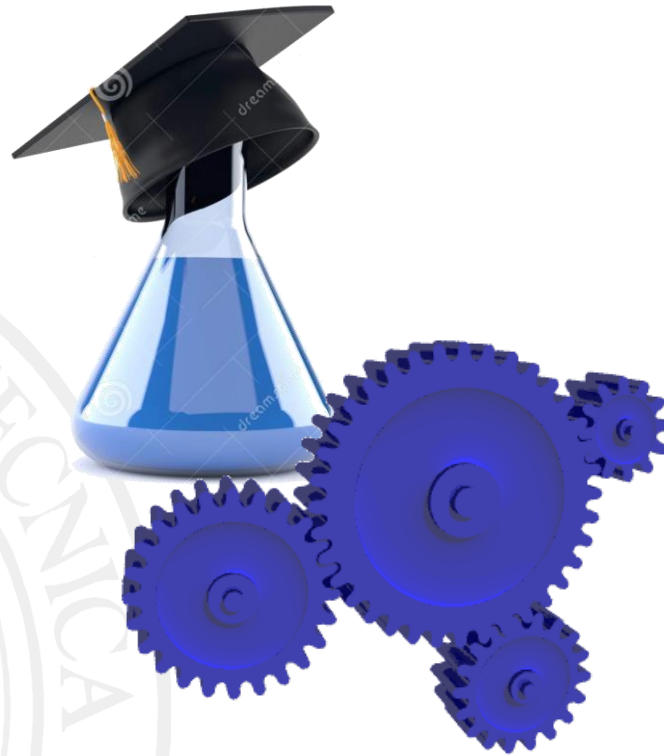
Romero, Trenor & Ferrero, Ann Biomed Eng 2009

Esquema de exposición

BASE TEÓRICA: Modelos computacionales de la actividad bioeléctrica del corazón

INVESTIGACIÓN: Análisis de los mecanismos arritmogénicos de la isquemia miocárdica

DESARROLLO: Simulación personalizada de ablación por RF en pacientes con infarto de miocardio



Isquemia aguda e infarto de miocardio

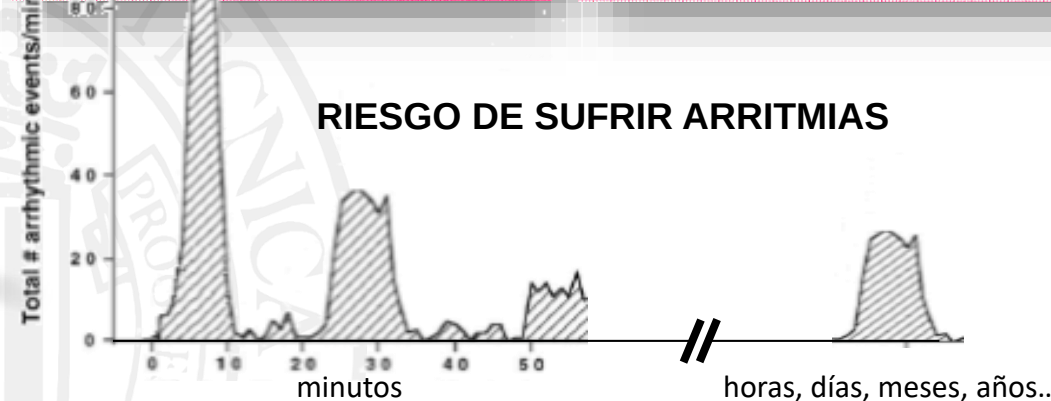
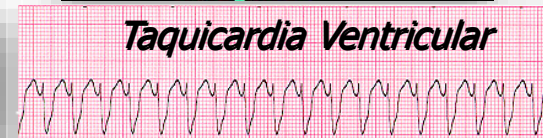
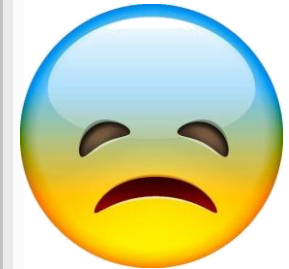
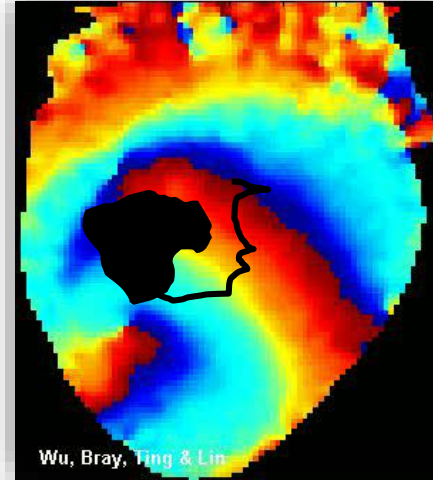
0-30 min: ISQUEMIA AGUDA

[Gray et al., 1995]



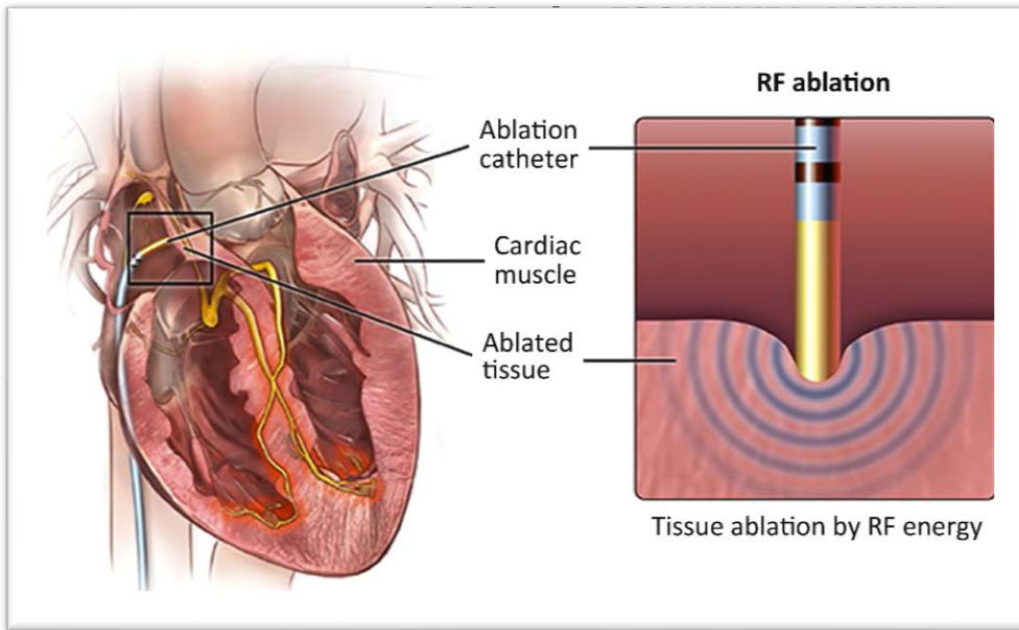
30 min →: INFARTO

[Wu et al, 2006]



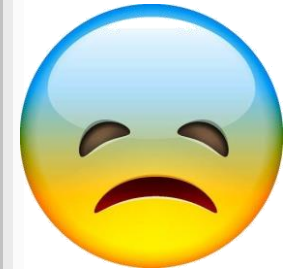
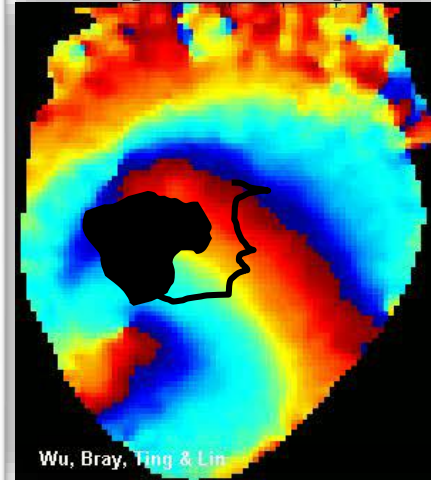
[Smith et al,1995]

Isquemia aguda e infarto de miocardio

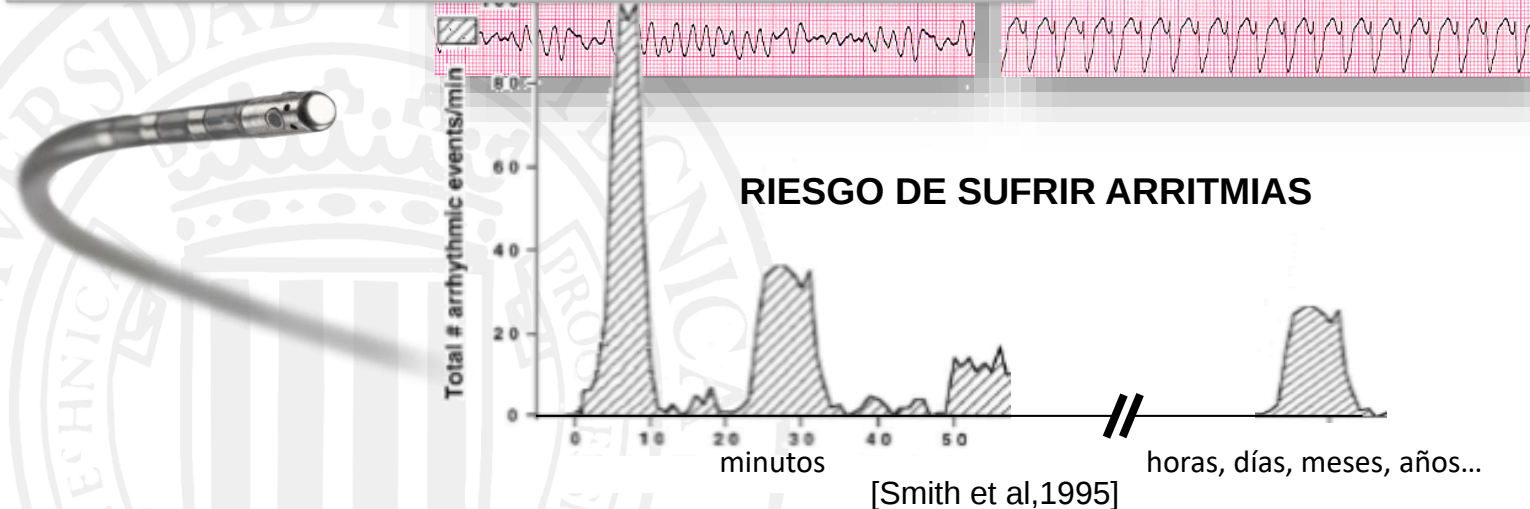


30 min →: INFARTO

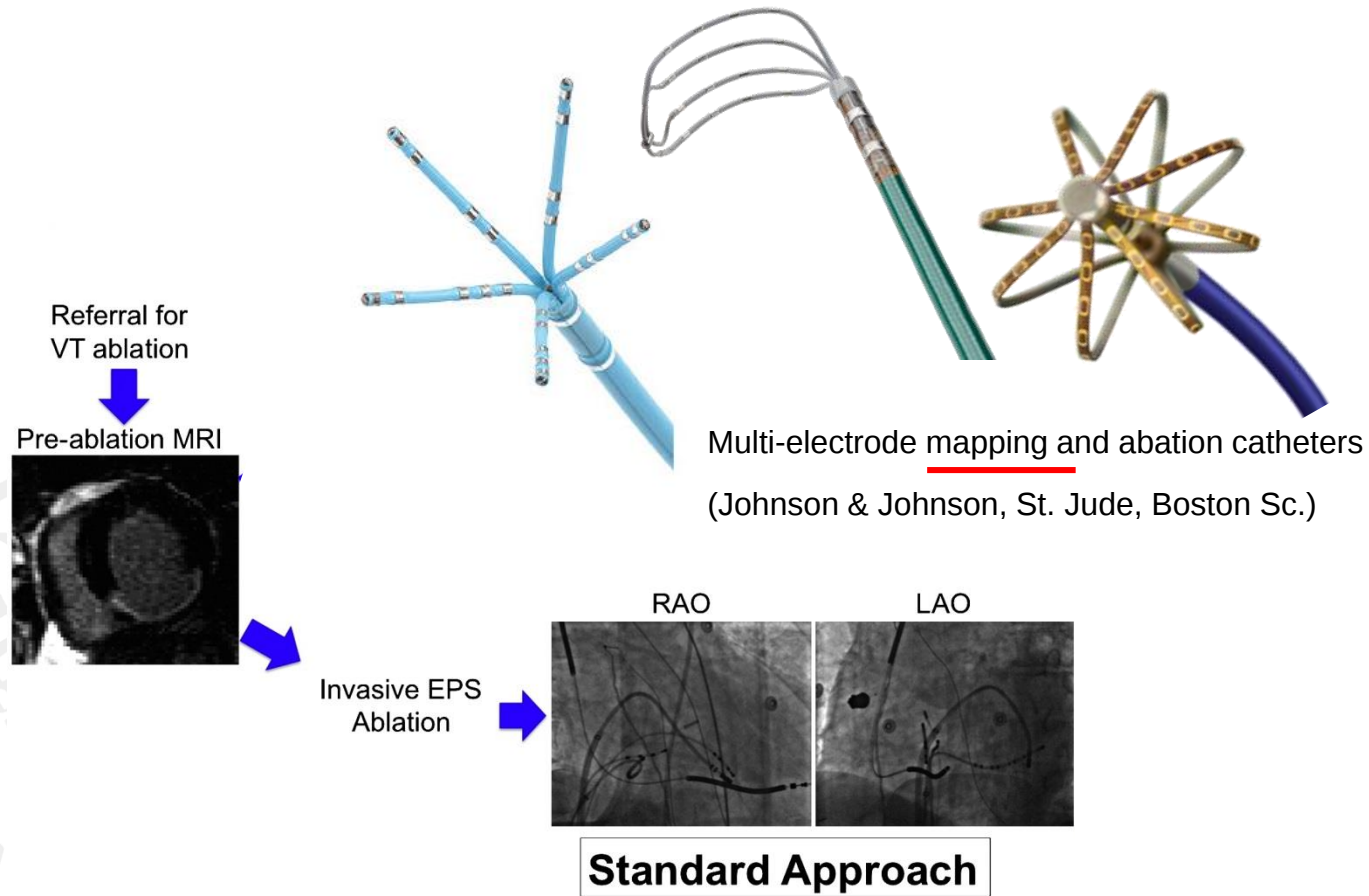
[Wu et al, 2006]



Taquicardia Ventricular



Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia



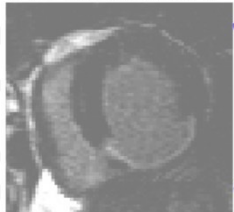
[adapted from Ashikaga et al, *Heart Rhythm* 2013]

Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia



Referral for
VT ablation

Pre-ablation MRI



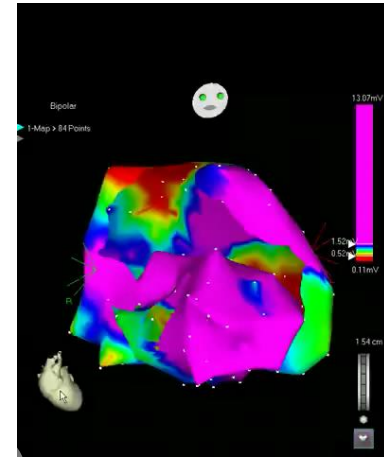
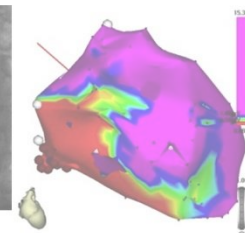
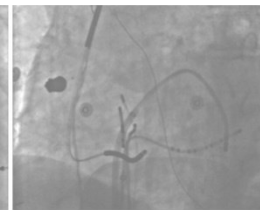
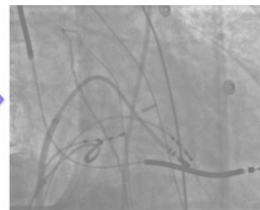
Invasive EPS
Ablation



RAO

LAO

CARTO



Standard Approach

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

Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

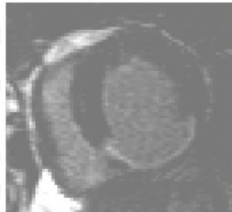
[courtesy of Dr. Ángel Ferrero, Hospital Clínic de Valencia]

INTELLA MIFI (Boston Sci.)

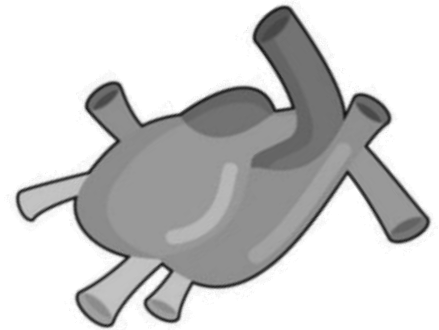
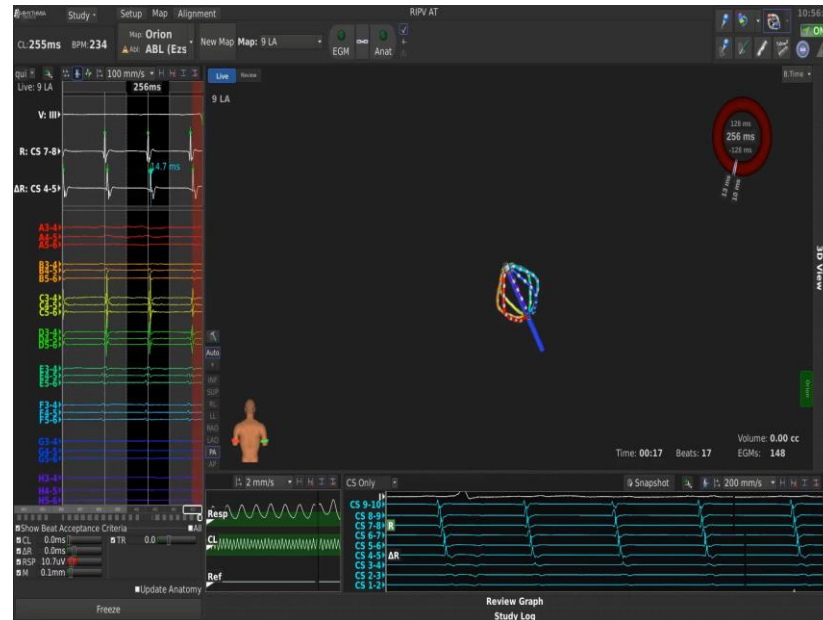


Referral for
VT ablation

Pre-ablation MRI



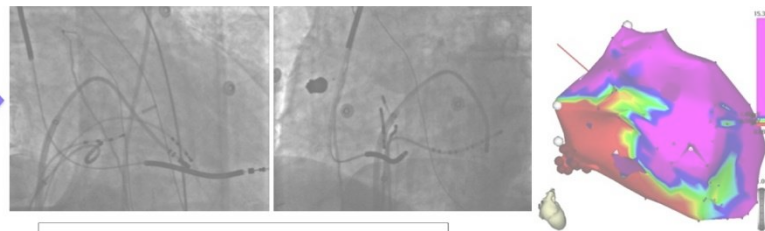
Invasive EPS
Ablation



RAO

LAO

CARTO

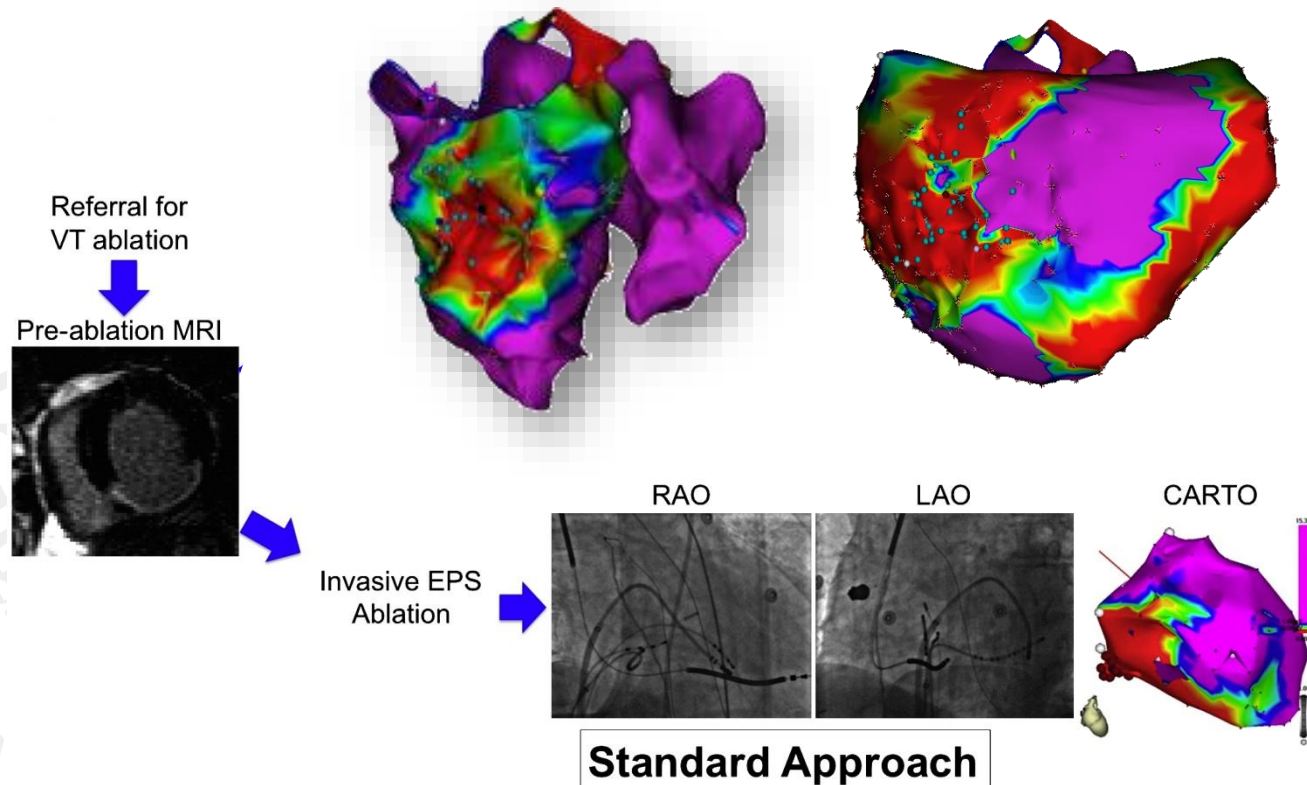


Standard Approach

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

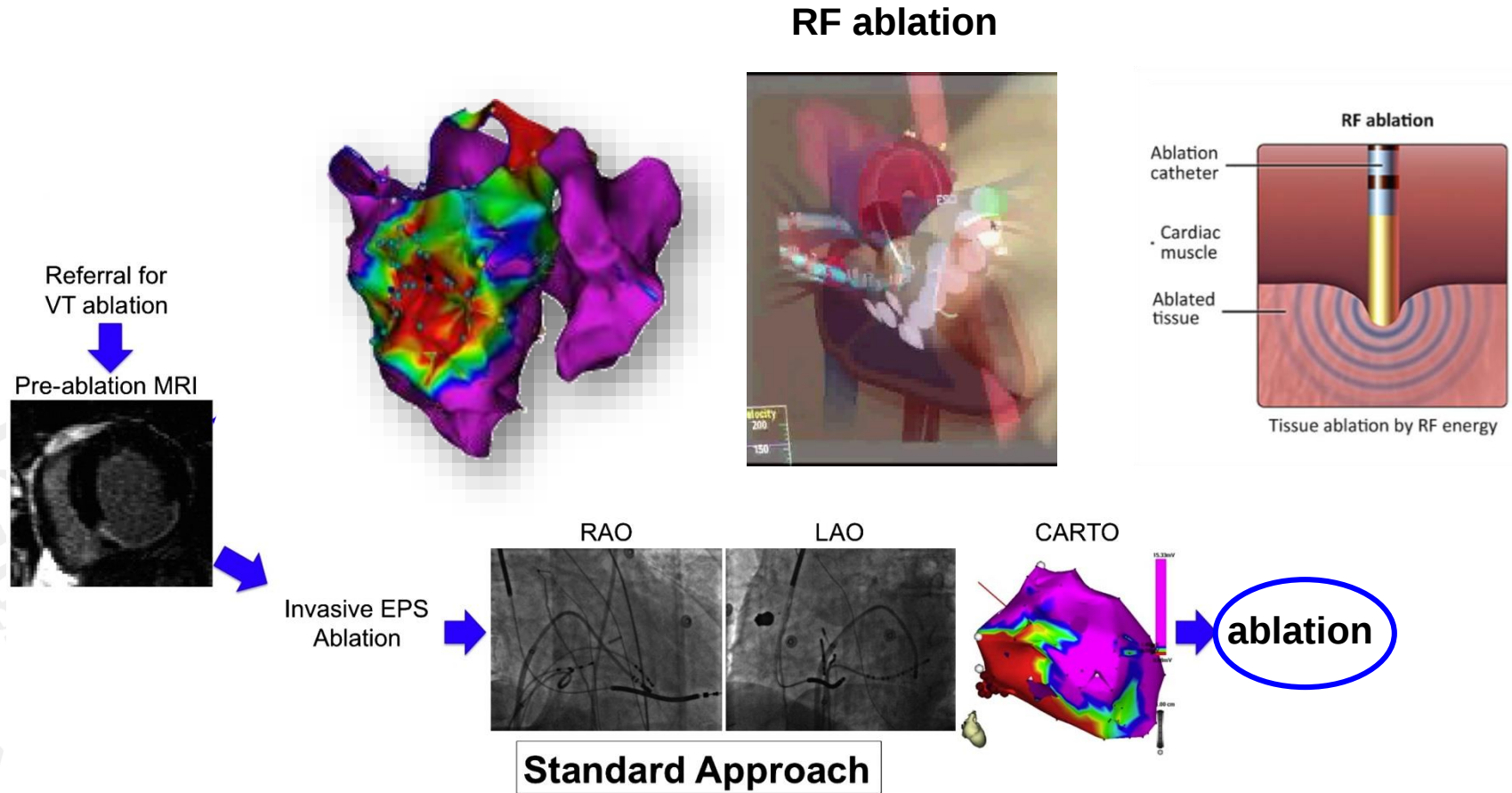
Radiofrequency ablation in patients with chronic myocardial infarction suffering ventricular tachycardia

Electroanatomical map of the endocardium...
... and the epicardium!



[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



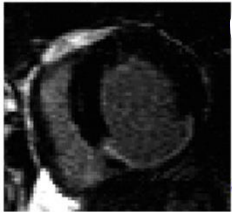
Alejandro Lopez-Perez^{1*}, Rafael Sebastian², M. Izquierdo^{3,4}, Ricardo Ruiz^{3,4}, Martin Bishop⁵ and Jose M. Ferrero¹

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 shows 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



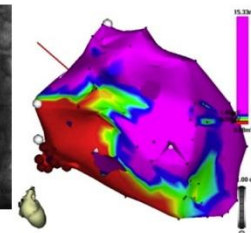
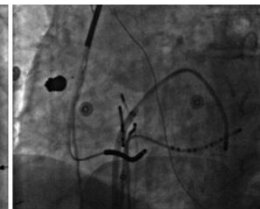
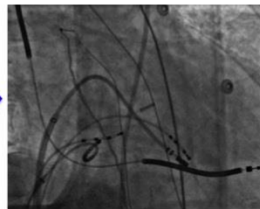
Invasive EPS
Ablation



RAO

LAO

CARTO



15.7mV
0

Standard Approach

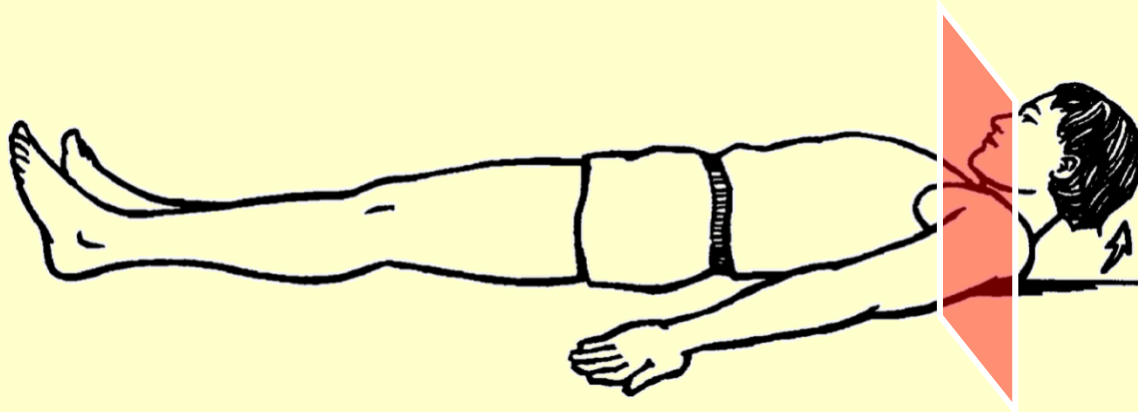
**optimal
ablation**



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

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

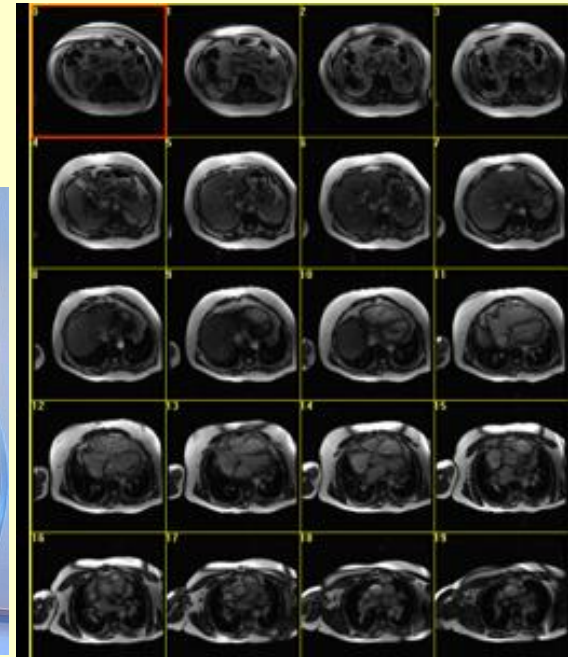
1. Geometría del corazón



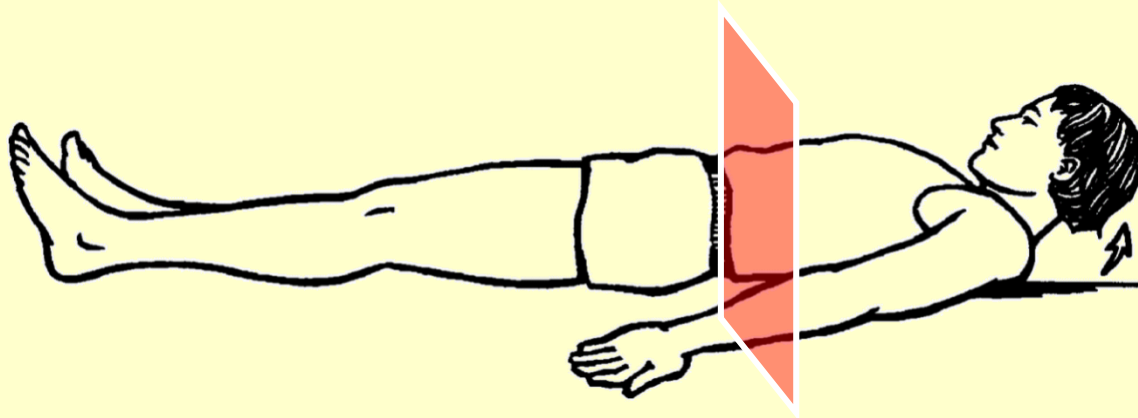
**Resonancia
Magnética Nuclear
(RMN – MRI)**



Imágenes de MRI

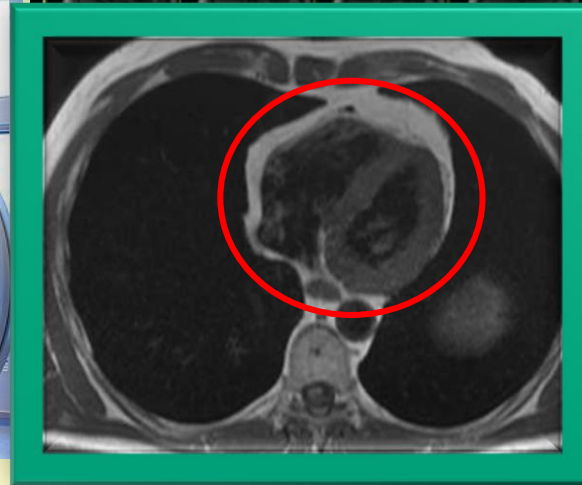
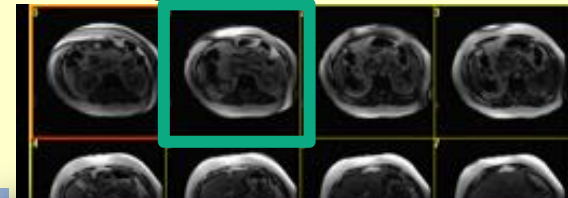


1. Geometría del corazón

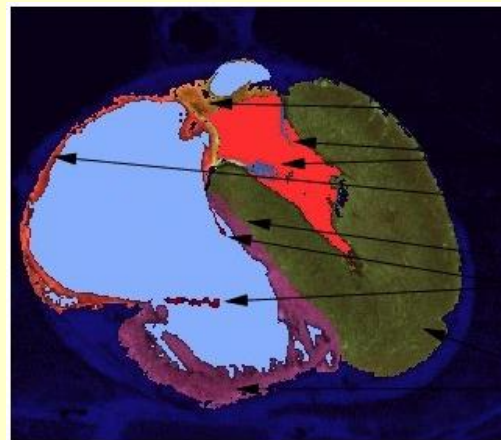


**Resonancia
Magnética Nuclear
(RMN – MRI)**

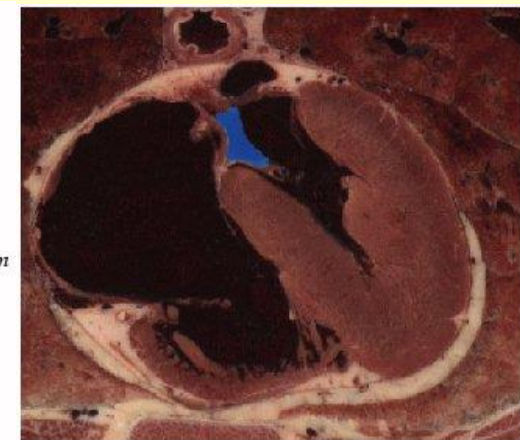
Imágenes de MRI



1. Geometría del corazón

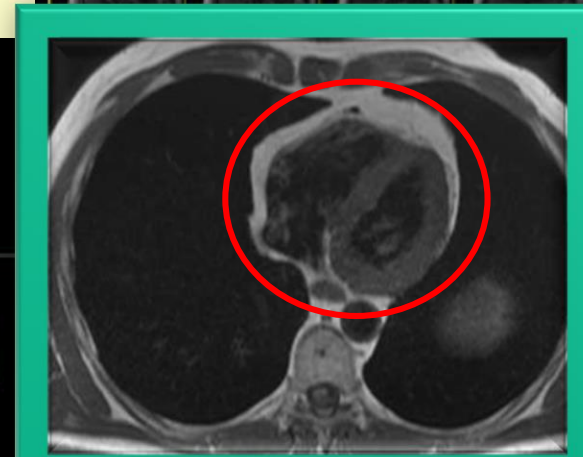
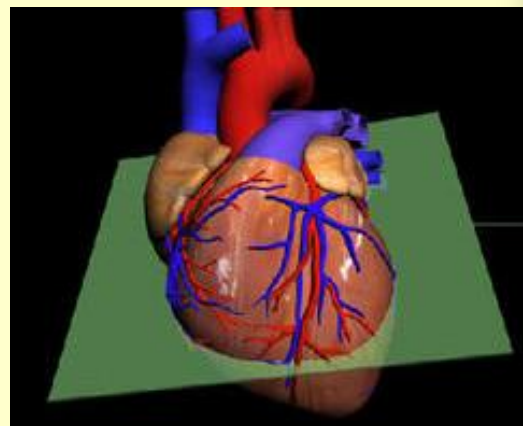
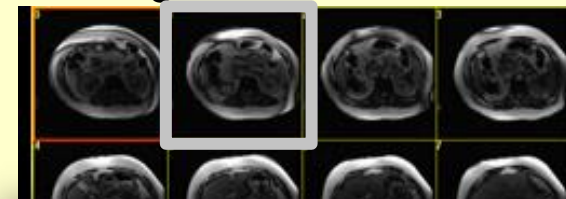


left atrium
tricuspid valve
right atrium
interventricular septum
mitral valve
left ventricle
right ventricle

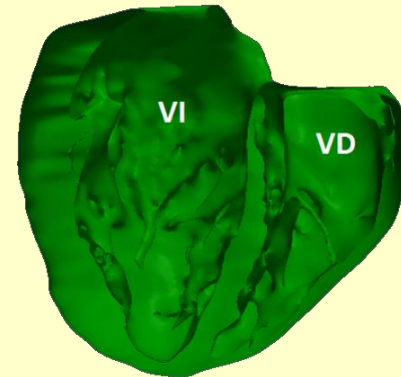
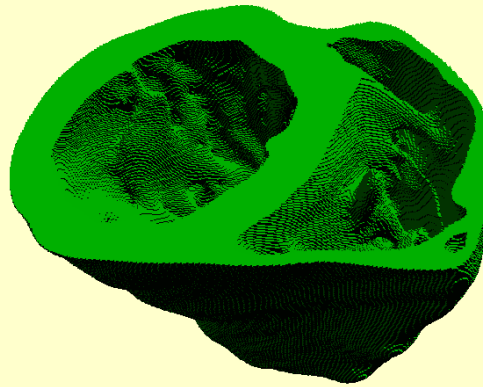
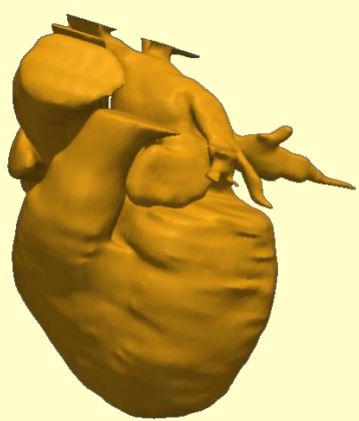


**Resonancia
Magnética Nuclear
(RMN – MRI)**

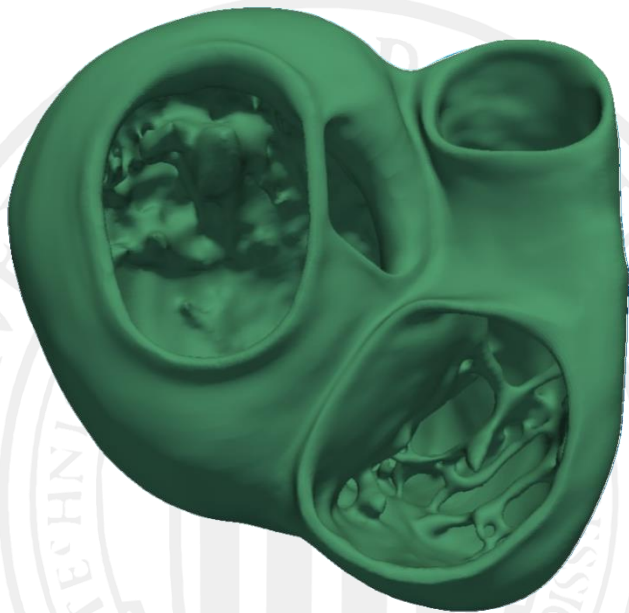
Imágenes de MRI



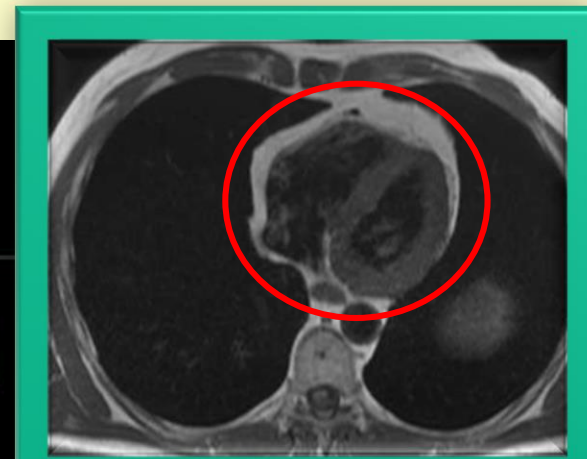
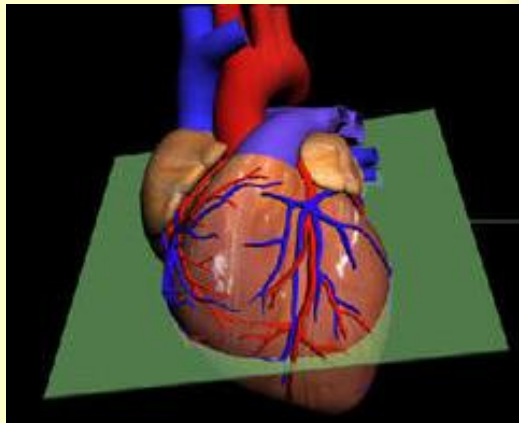
1. Geometría del corazón



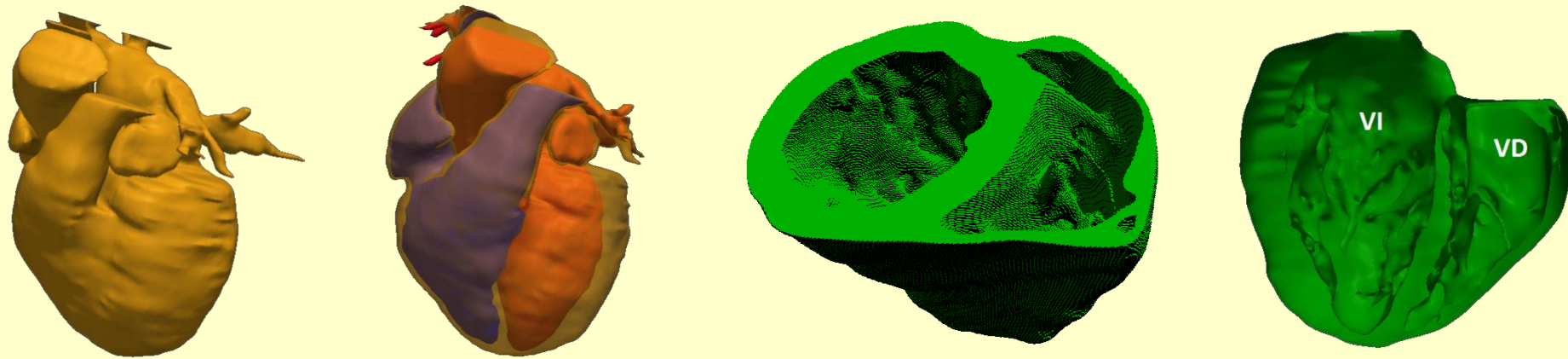
Endocardio “detallado”



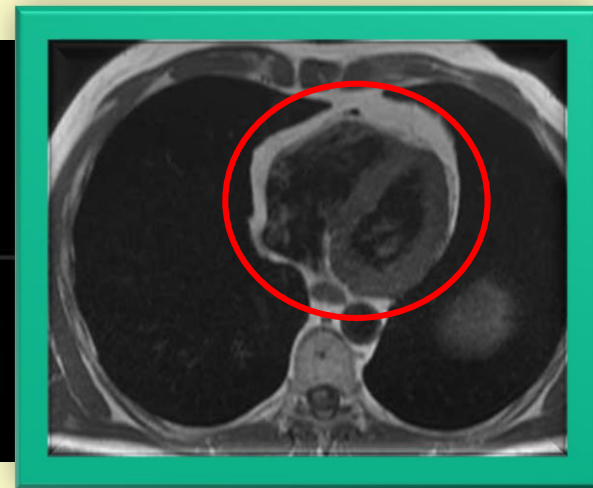
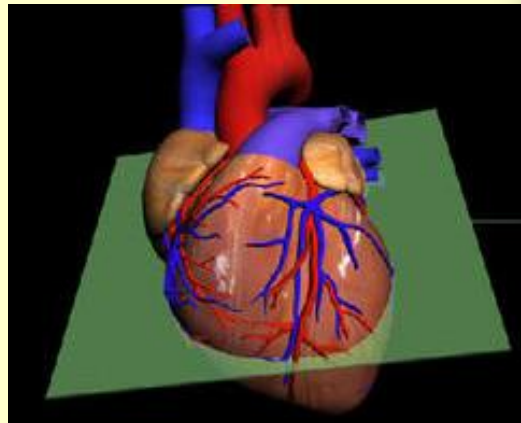
Imágenes de MRI



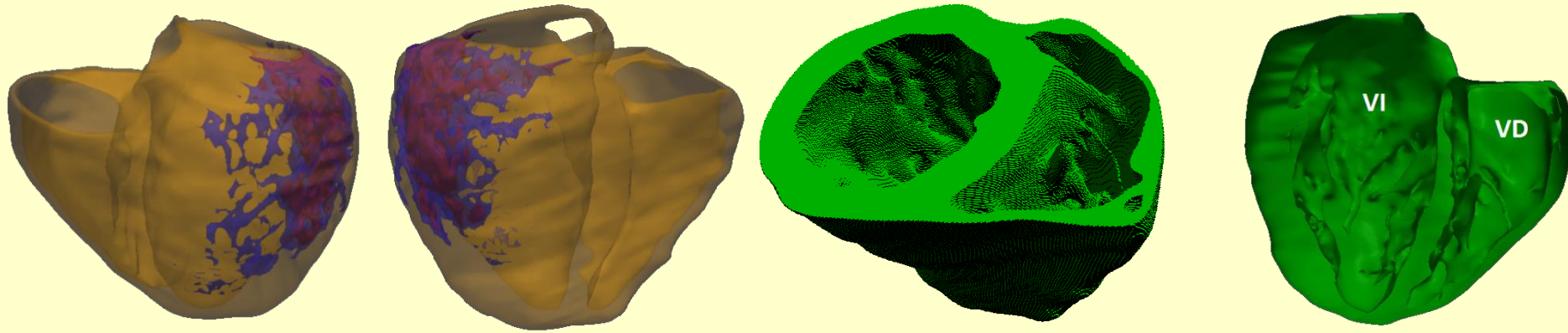
1. Geometría del corazón



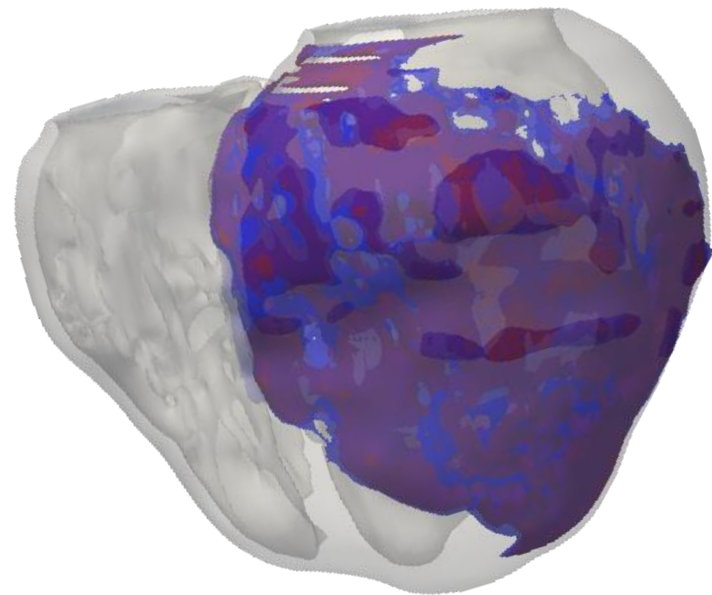
Imágenes de MRI



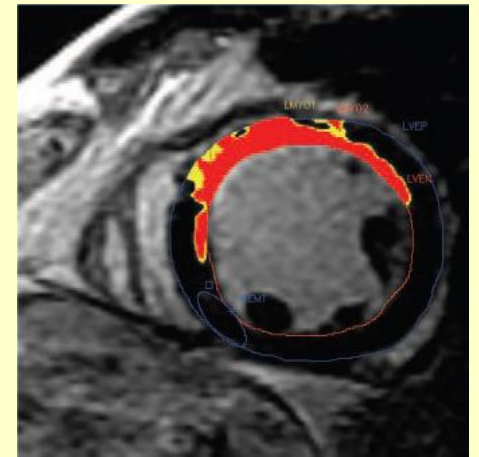
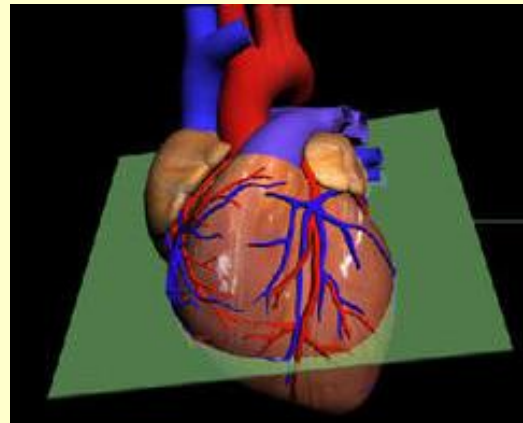
2. Cicatriz del infarto (núcleo + zona de borde)



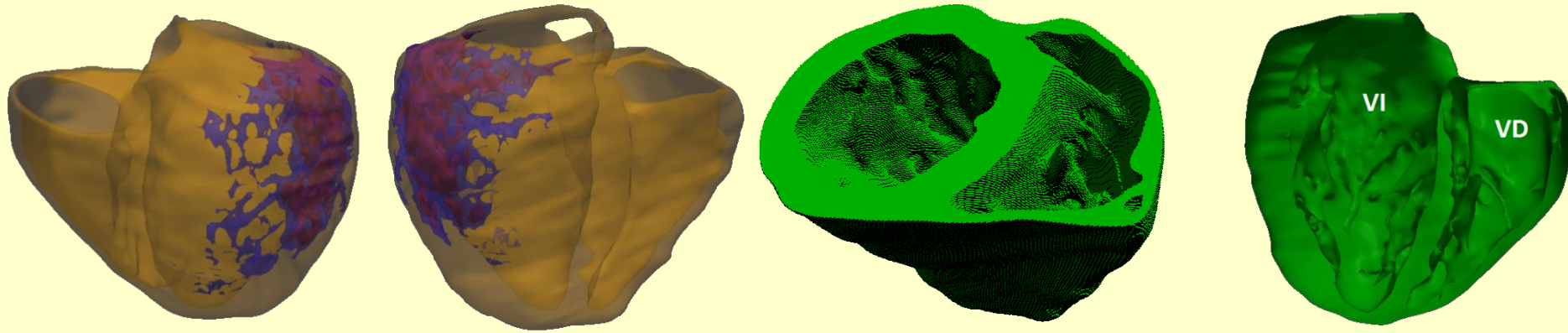
Cicatriz



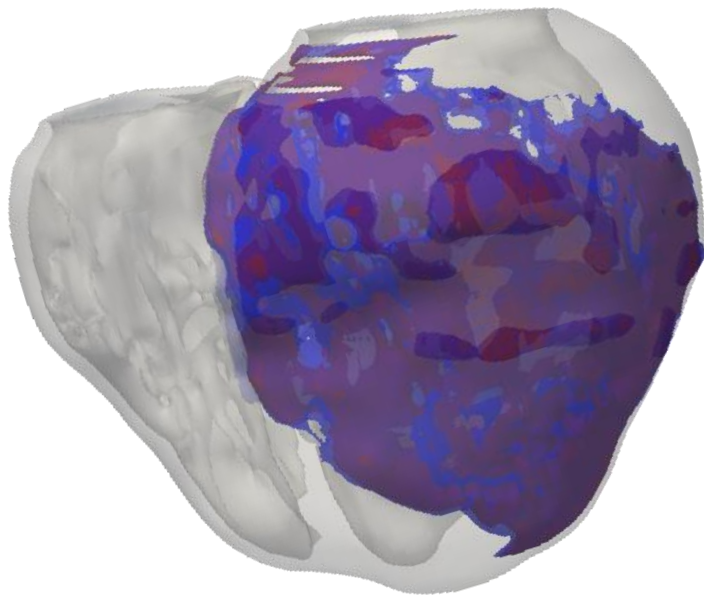
**Imágenes de MRI
(Delay enhancement)**



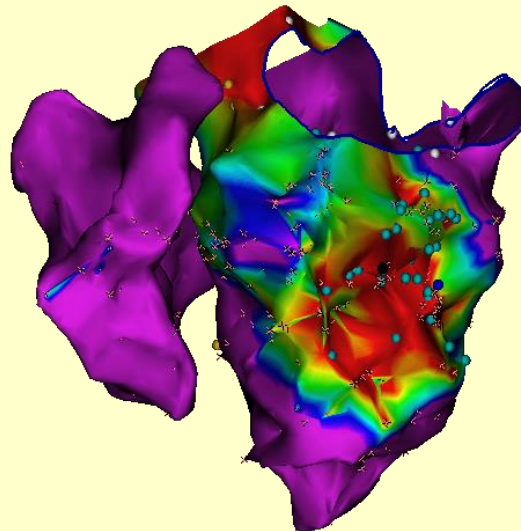
2. Cicatriz del infarto (núcleo + zona de borde)



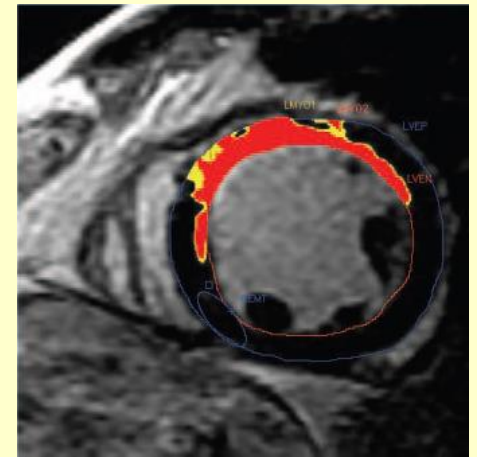
Cicatriz



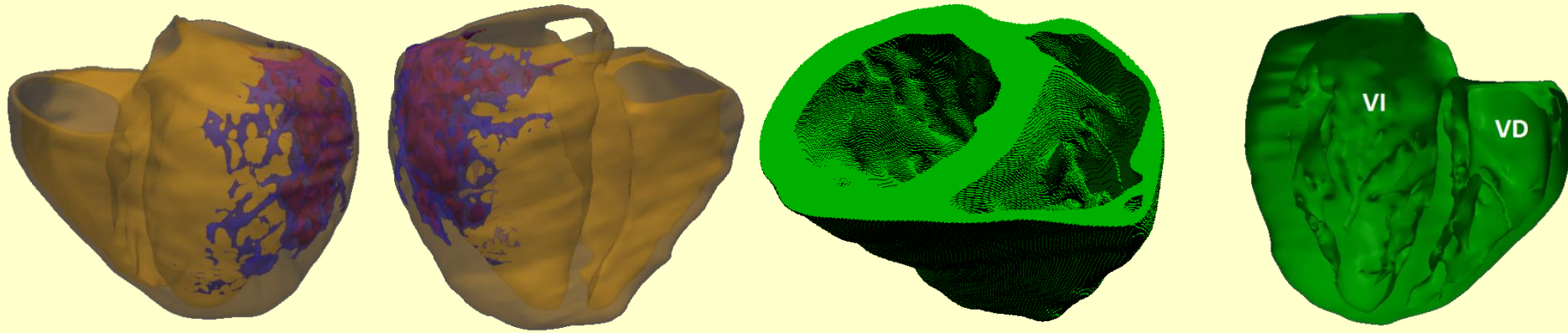
Mapa electro-anatómico (CARTO)



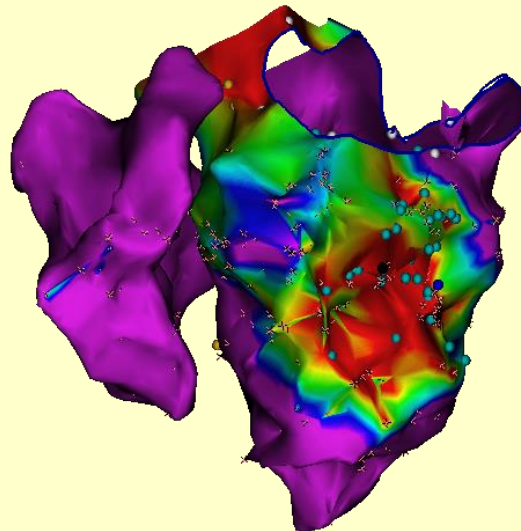
Imágenes de MRI (Delay enhancement)



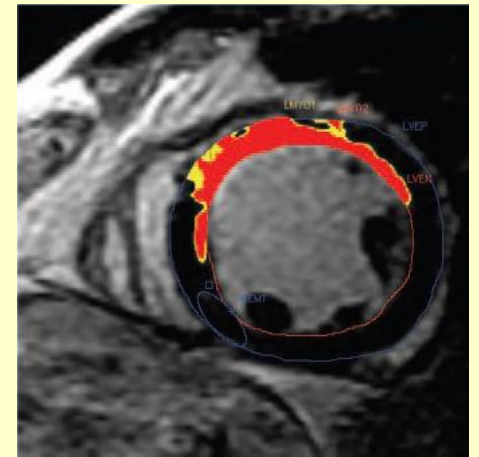
2. Cicatriz del infarto (núcleo + zona de borde)



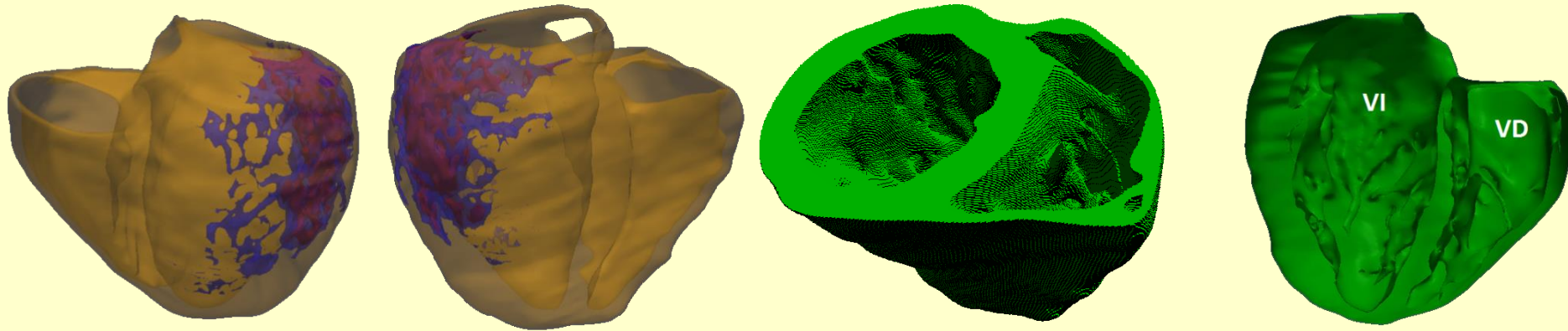
Mapa electro-anatómico (CARTO)



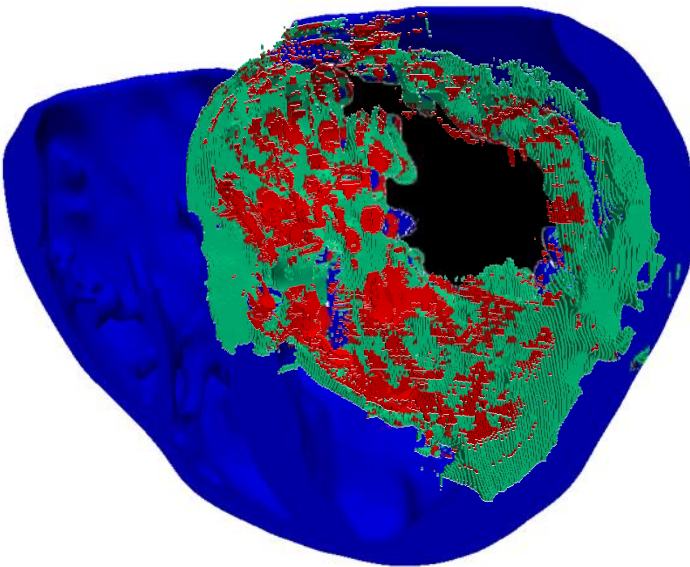
Imágenes de MRI (Delay enhancement)



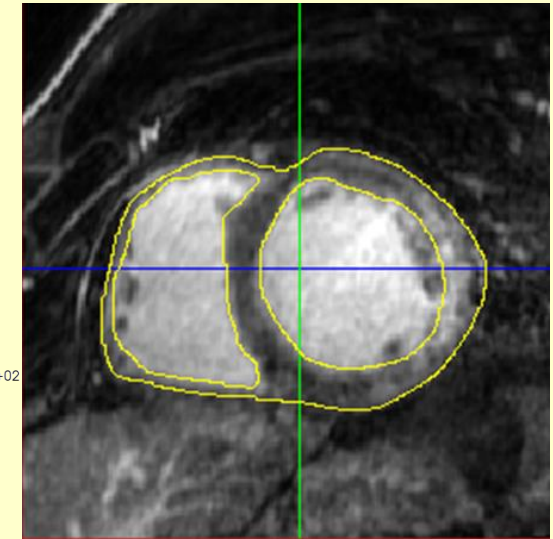
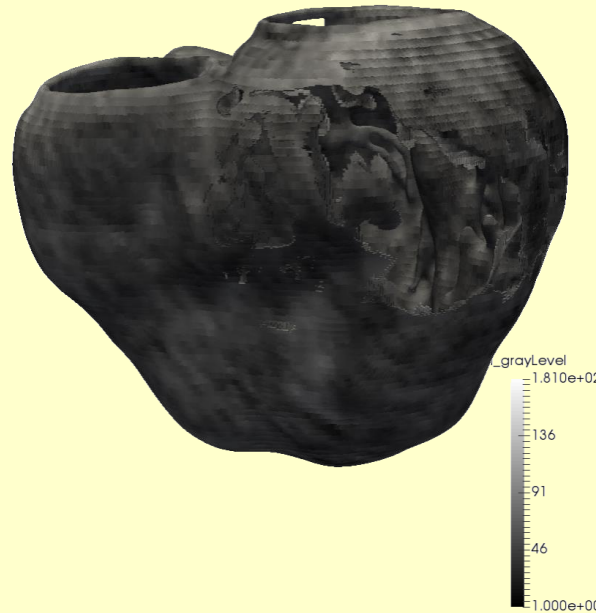
3. Fibrosis en la zona del infarto



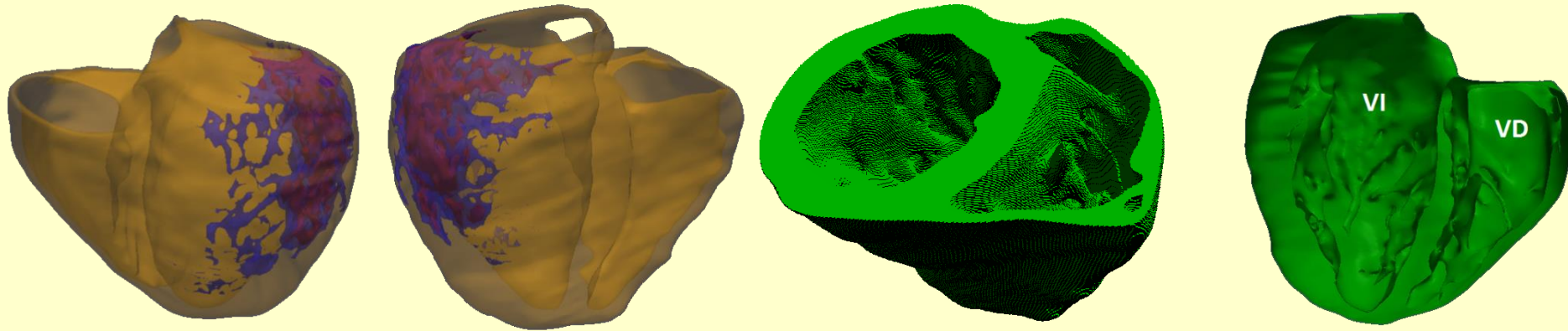
fibrosis



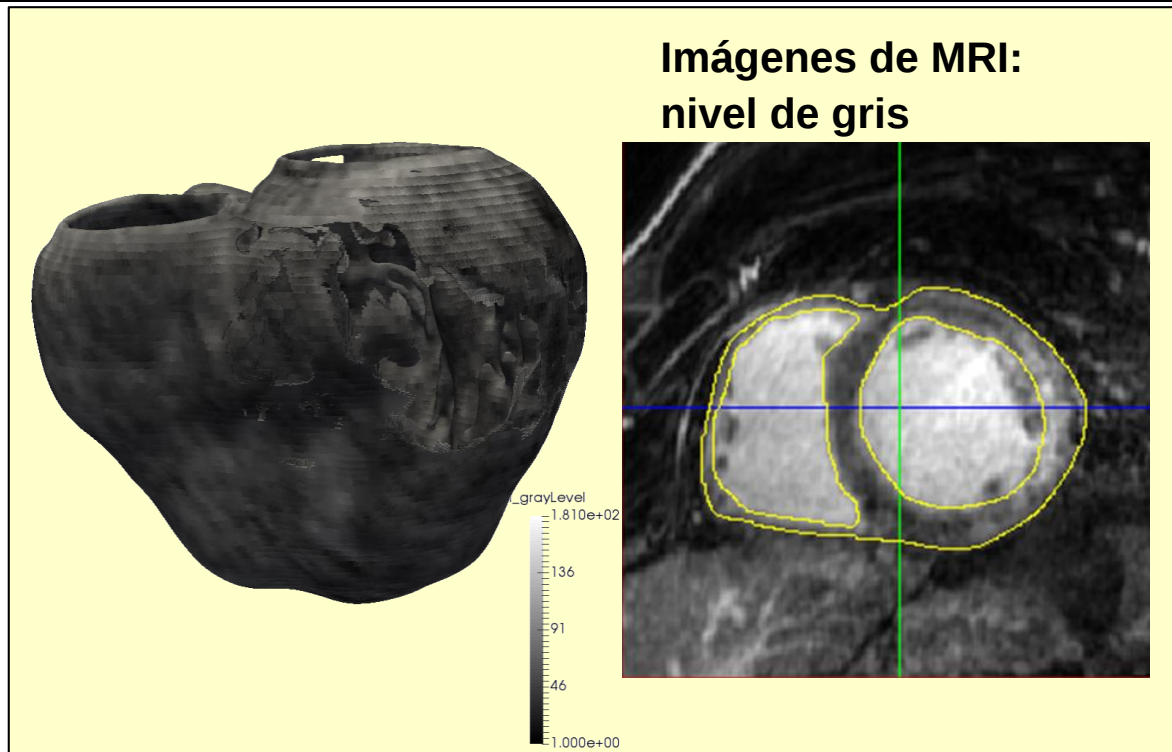
**Imágenes de MRI:
nivel de gris**



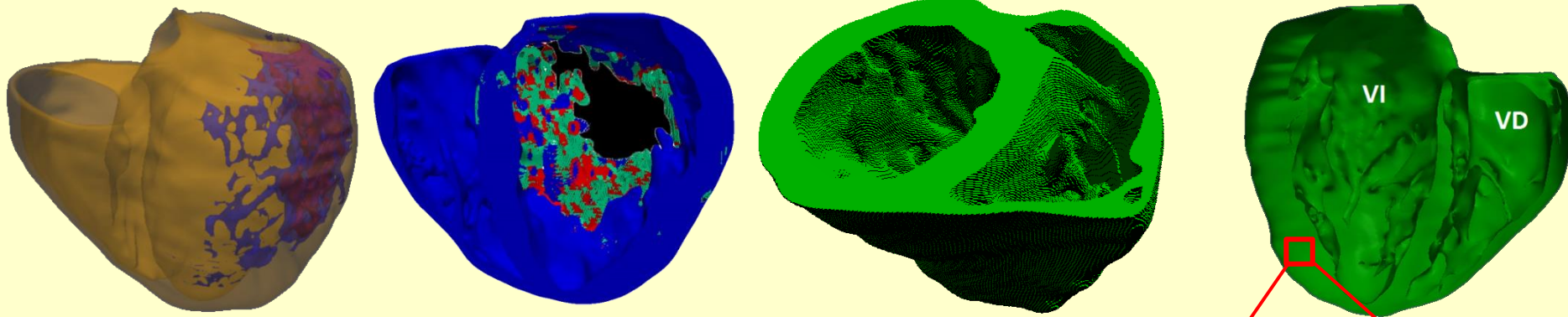
3. Fibrosis en la zona del infarto



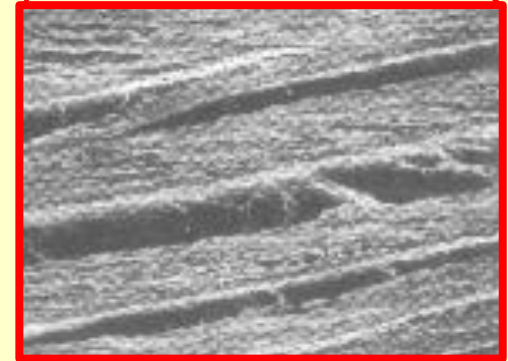
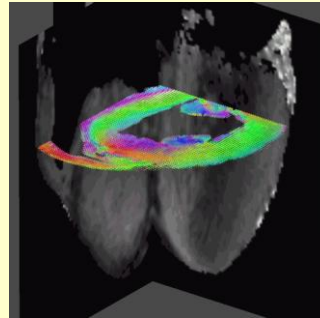
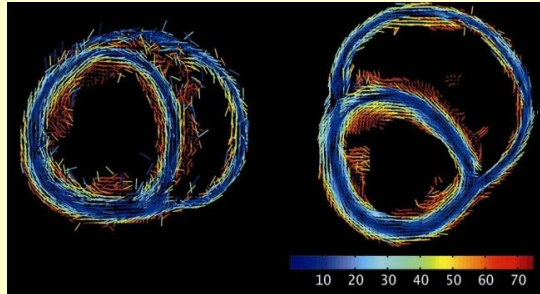
BASTANTE
Personalizable



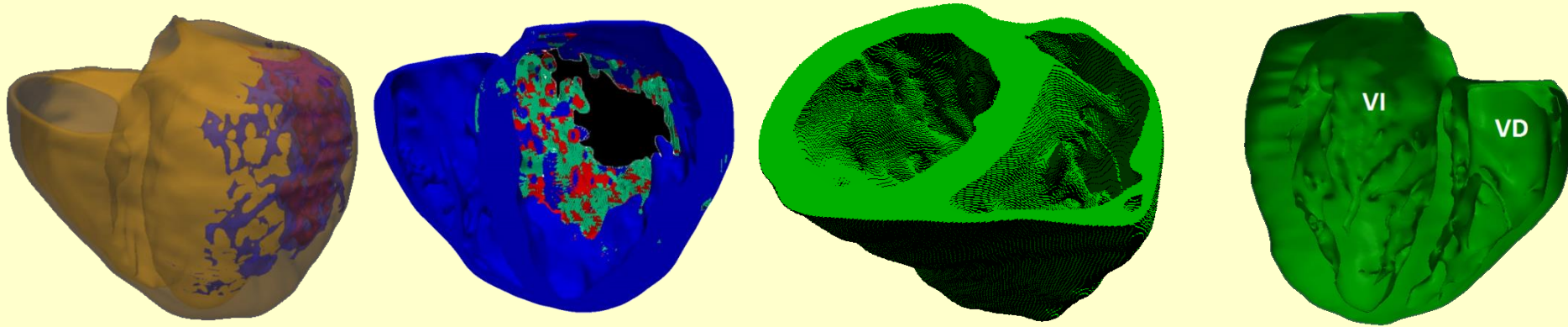
4. Estructura del miocardio (orientación de fibras)



MRI-DTI (*Diffusion Tensor Imaging*)



4. Estructura del miocardio (orientación de fibras)



Orientación de fibras: estimación

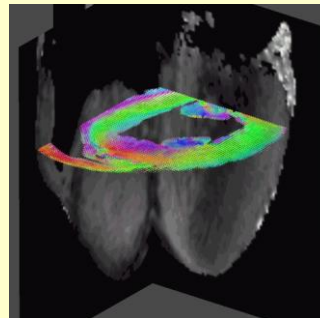
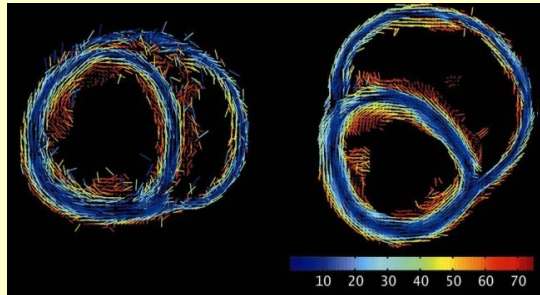
Rule-based method

DTI

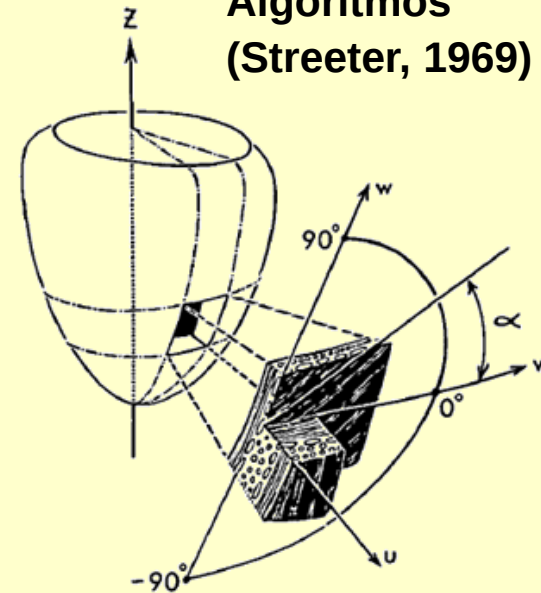
Epi

Endo

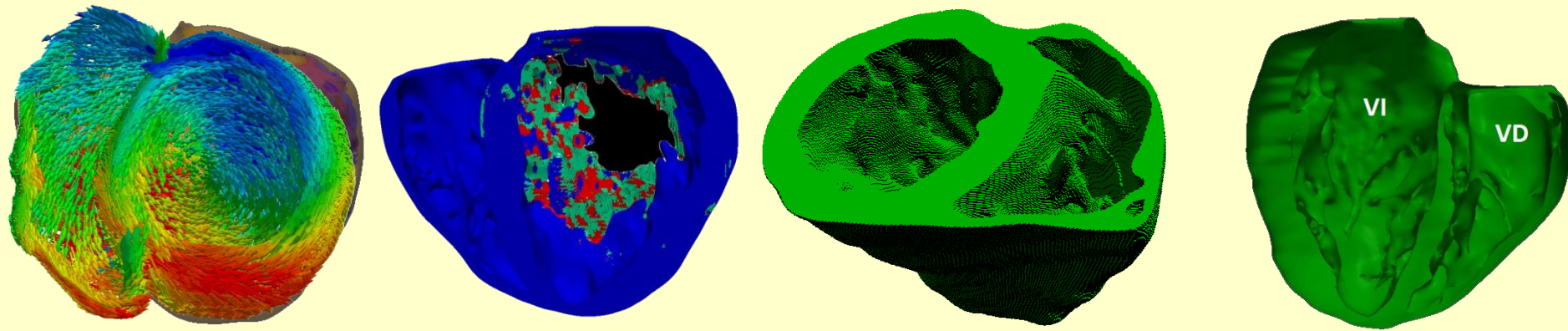
MRI-DTI (Diffusion Tensor Imaging)



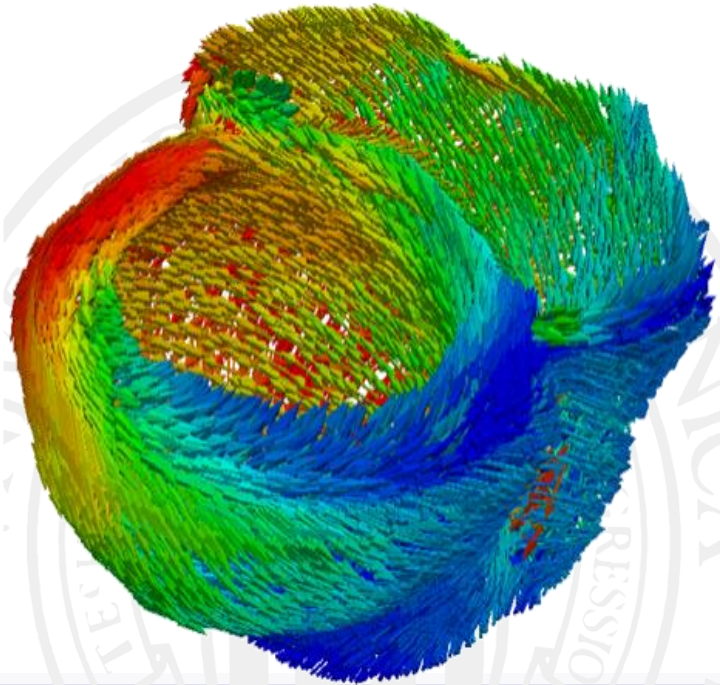
Algoritmos (Streeter, 1969)



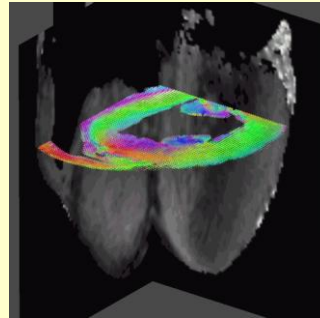
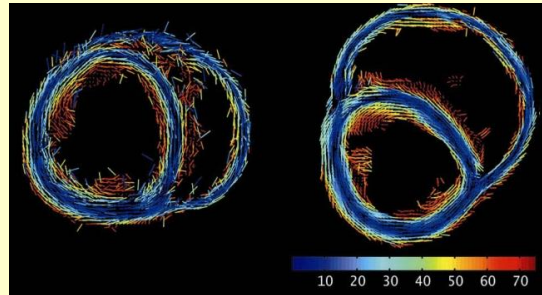
4. Estructura del miocardio (orientación de fibras)



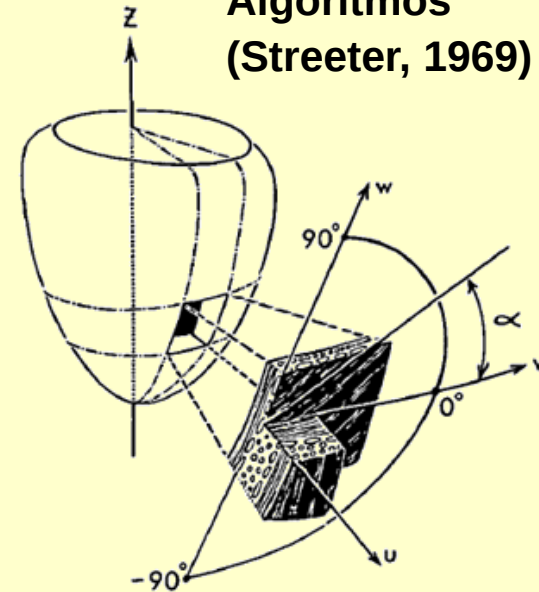
Estimación de la orientación de fibras



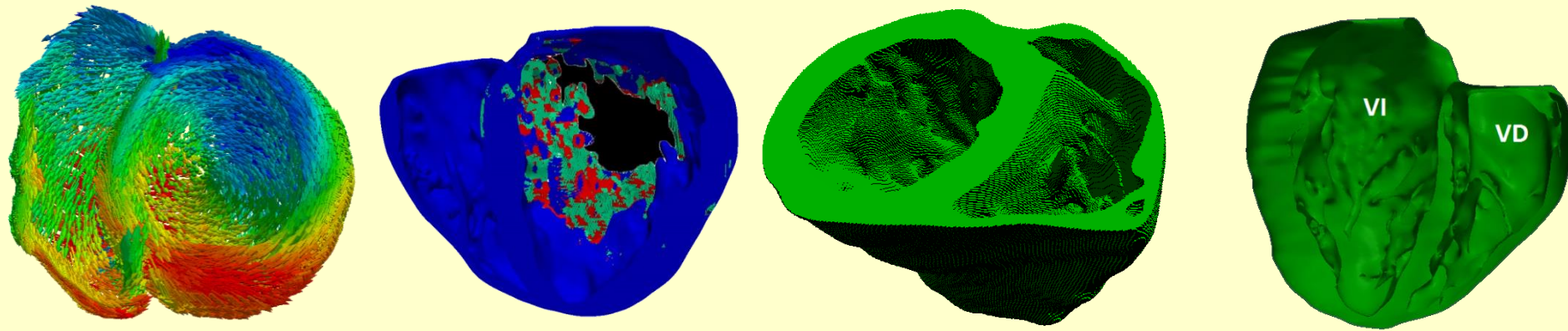
MRI-DTI (*Diffusion Tensor Imaging*)



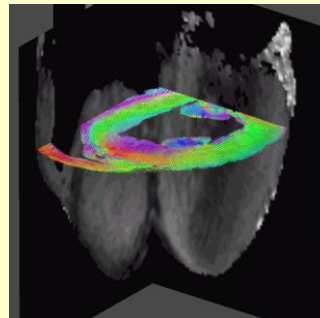
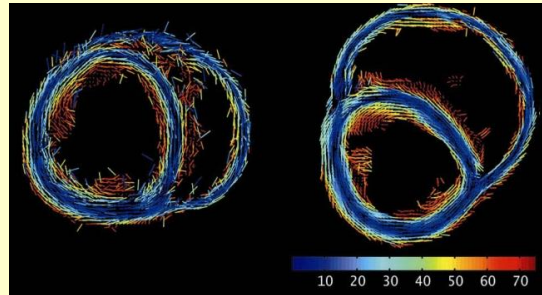
Algoritmos (Streeter, 1969)



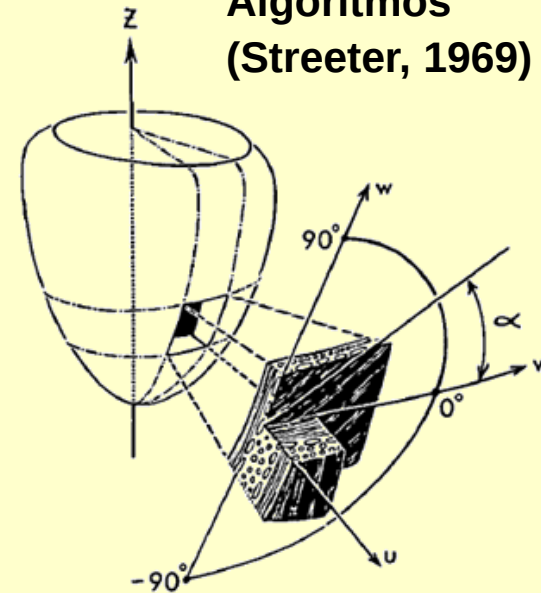
4. Estructura del miocardio (orientación de fibras)



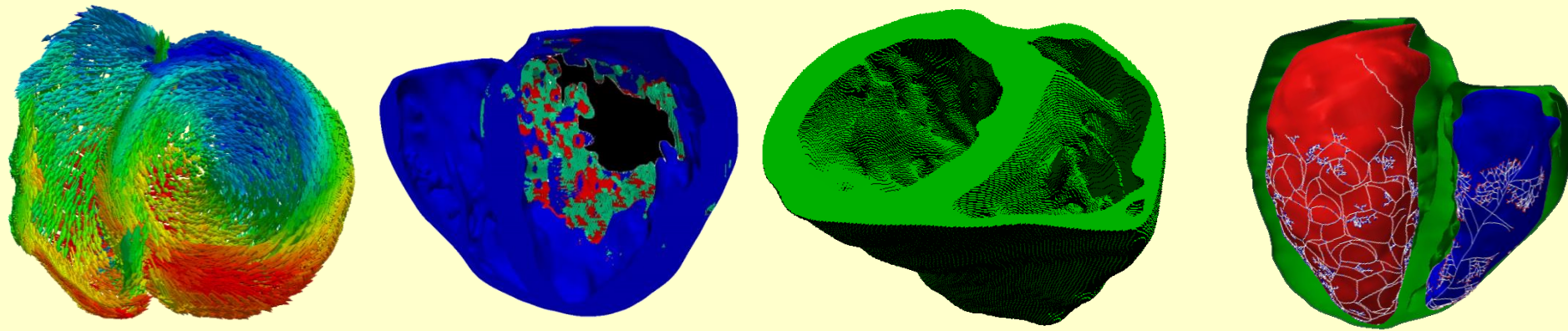
MRI-DTI (*Diffusion Tensor Imaging*)



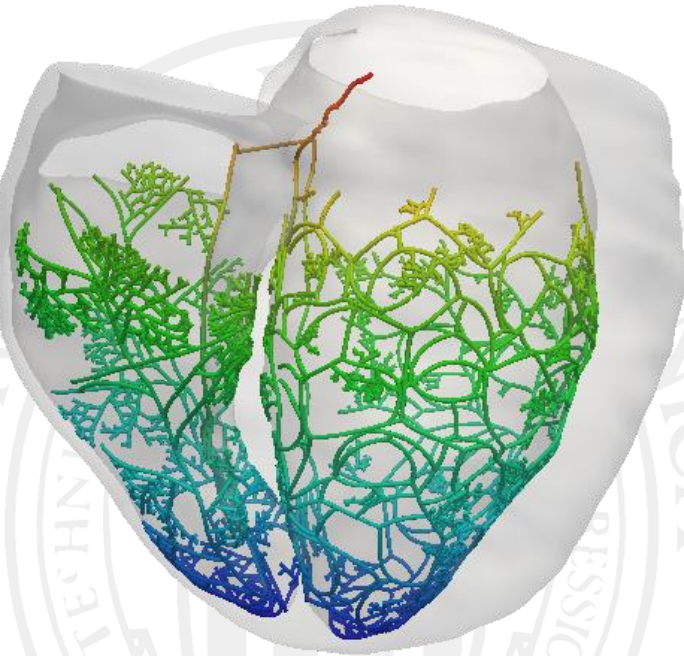
Algoritmos (Streeter, 1969)



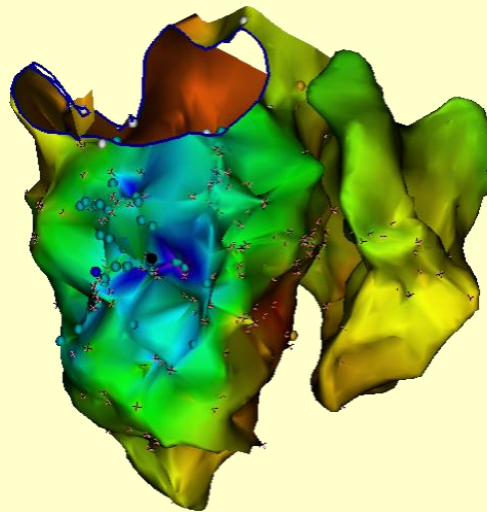
5. Sistema de conducción (His-Purkinje)



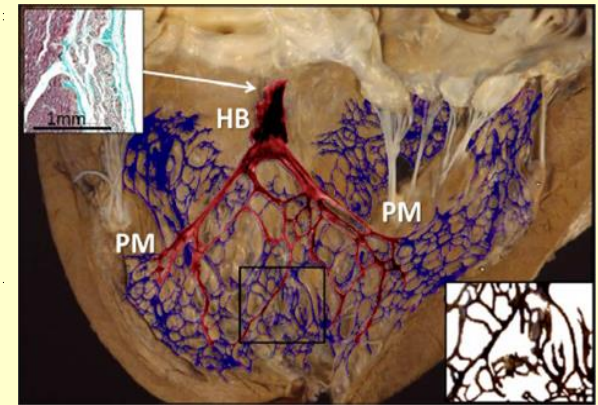
Estimación inversa del árbol de Purkinje



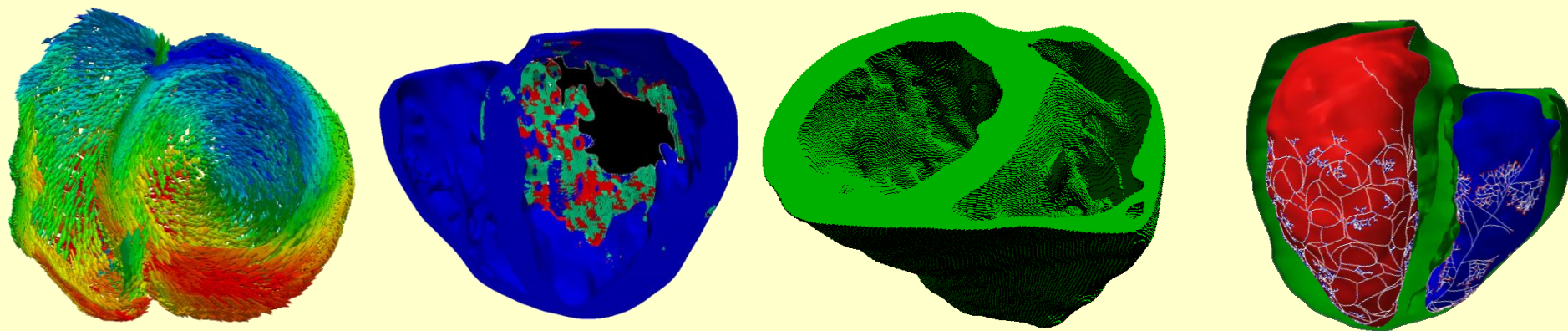
Mapa electro-anatómico
(CARTO) [LAT]



Fotografías/Atlas



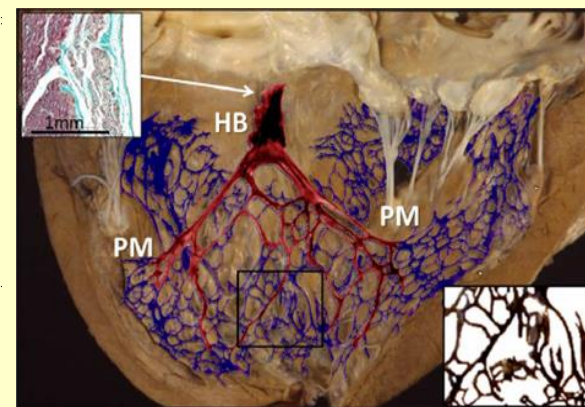
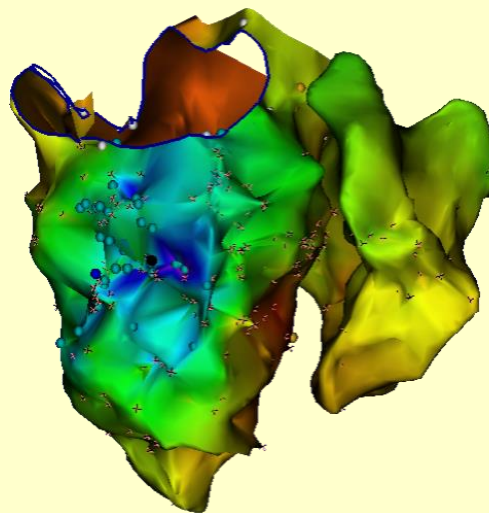
5. Sistema de conducción (His-Purkinje)



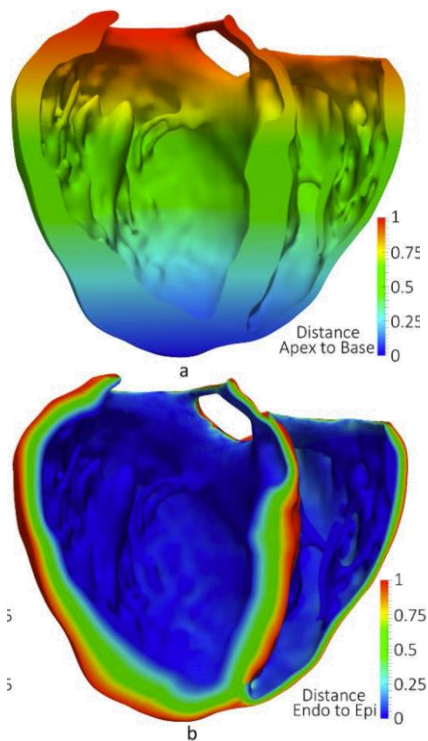
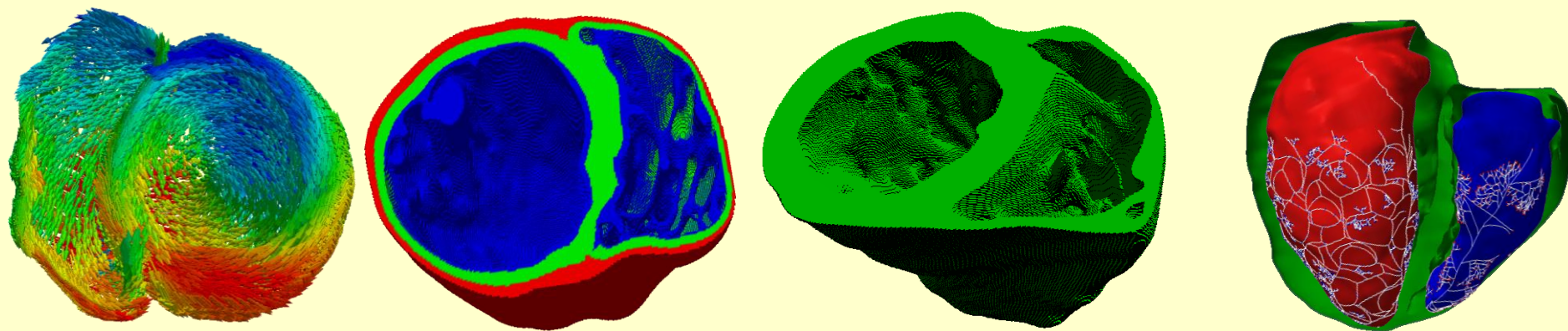
RELATIVA-
MENTE
Personalizable

Mapa electro-anatómico
(CARTO) [LAT]

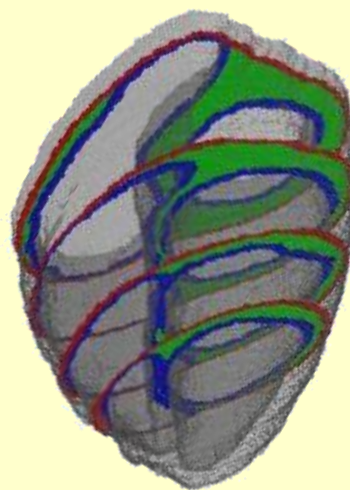
Fotografías/Atlas



6. Heterogeneidad electrofisiológica



Heterogeneidad transmural



Epicardio

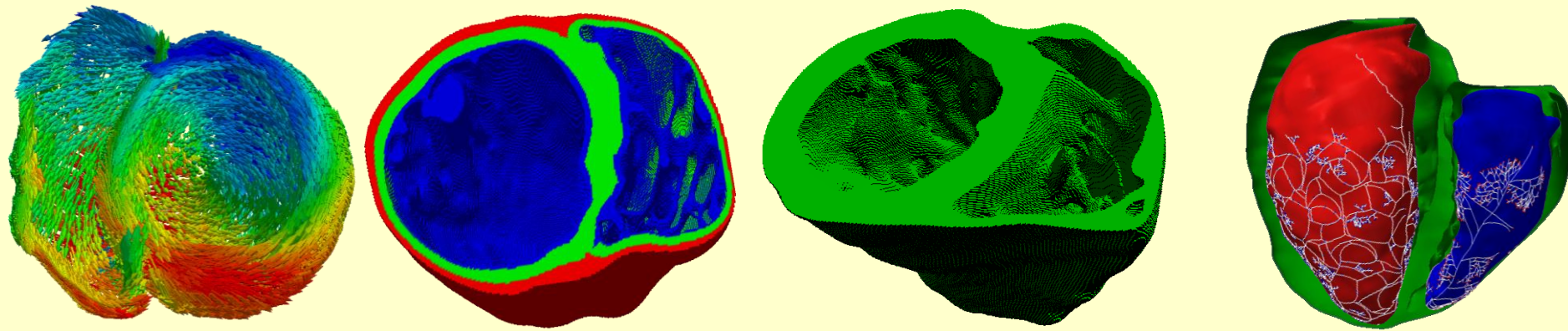
Midmiocardio

Endocardio

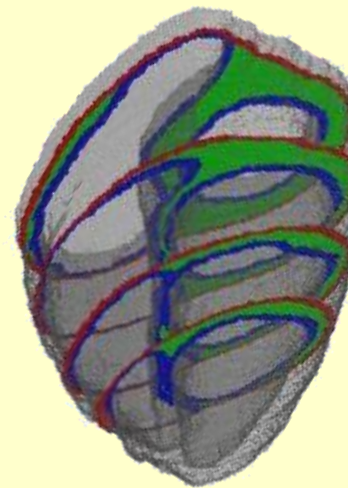


(Liu & Antzelevitch 1993)

6. Heterogeneidad electrofisiológica

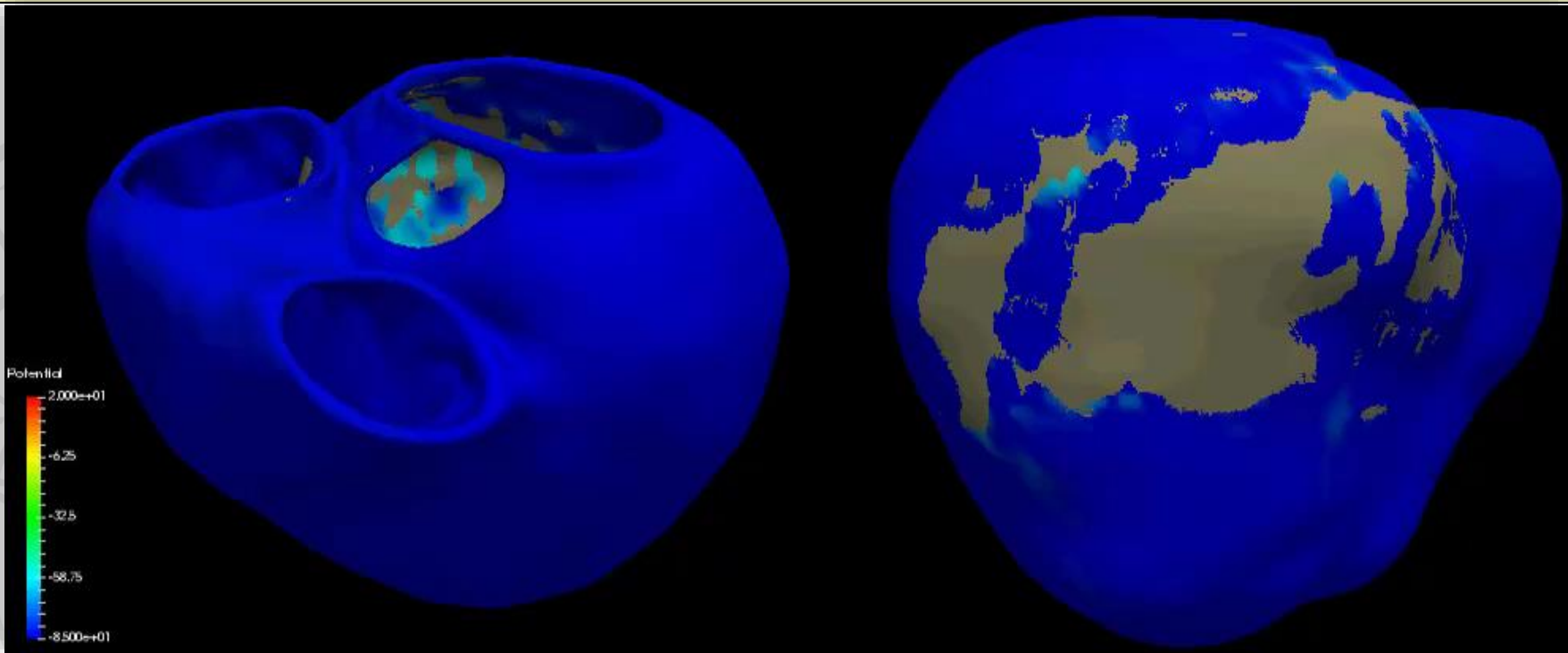
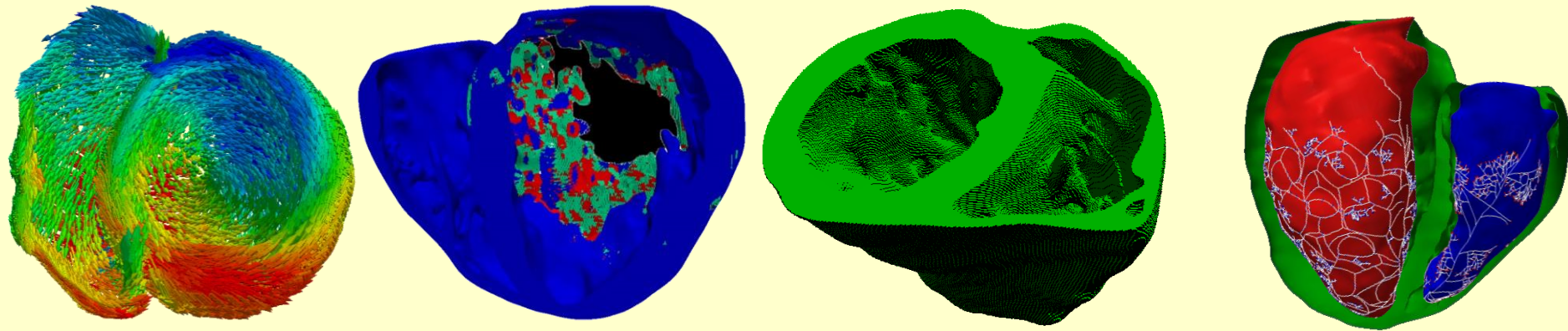


Heterogeneidad transmural

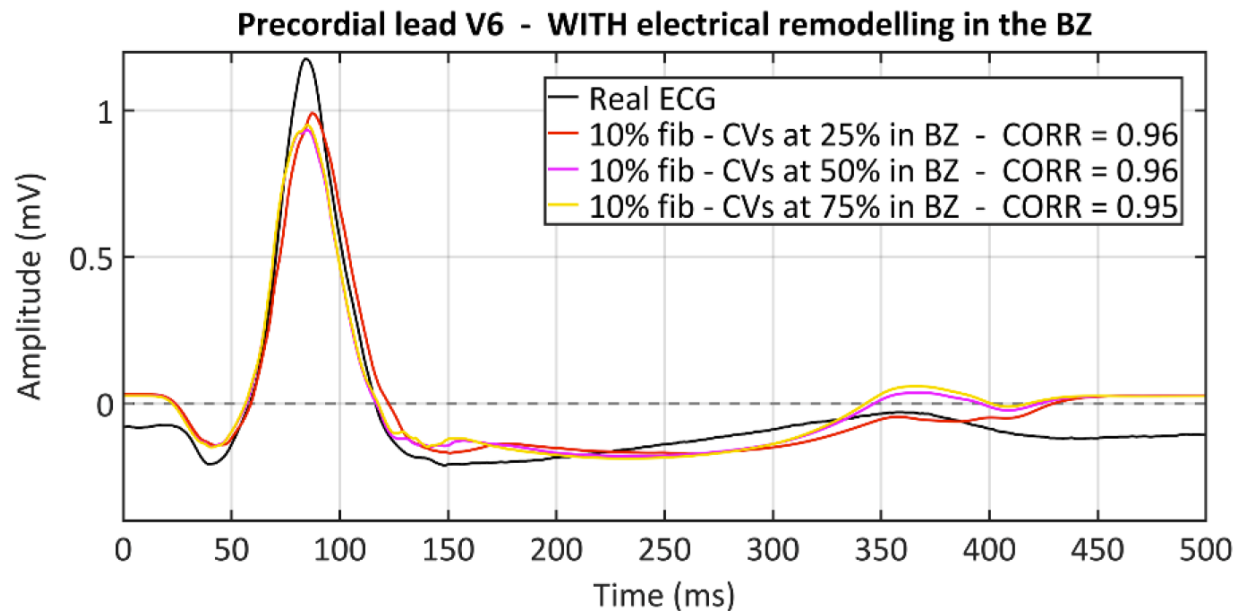
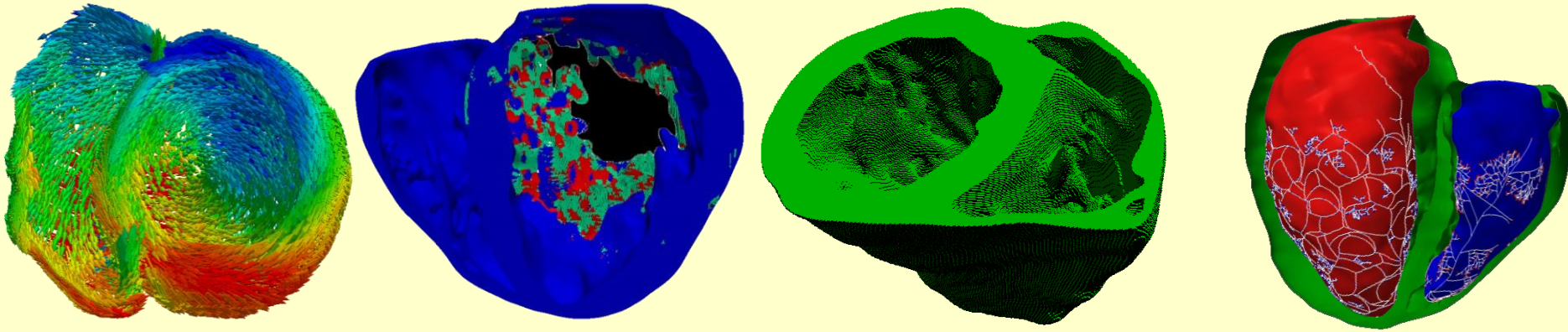


(Liu & Antzelevitch 1993)

Simulación (ritmo sinusal → taquicardia ventricular)

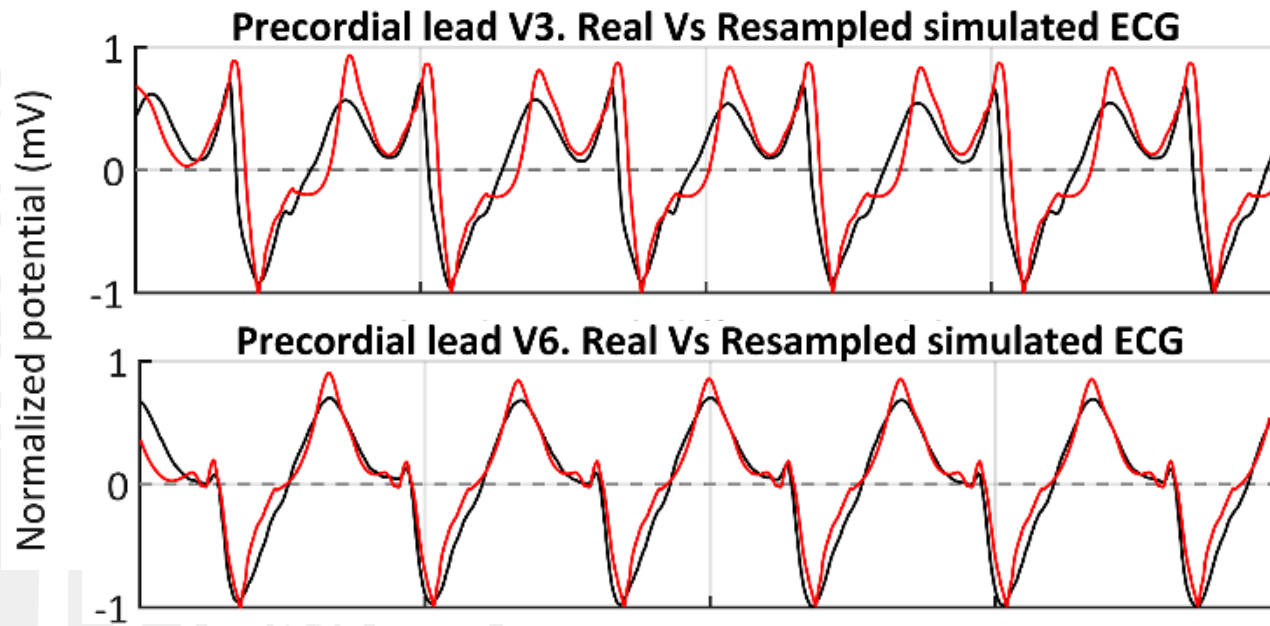
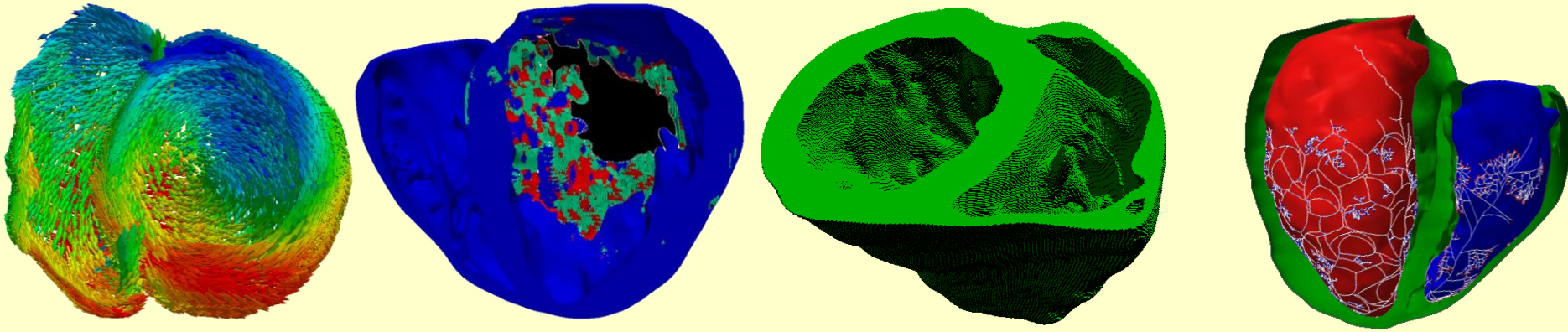


Simulación (corazón infartado, ritmo sinusal) [ECG]



López-Pérez, Sebastián, Izquierdo, Ruiz, Bishop & Ferrero, *Front. In Physiol.* (Frontiers in Physiology, 2019)

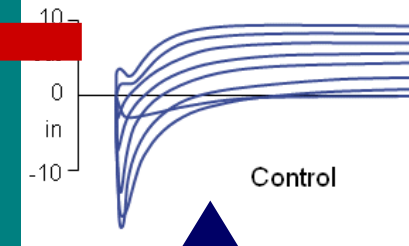
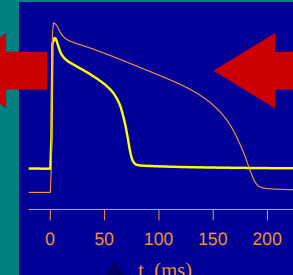
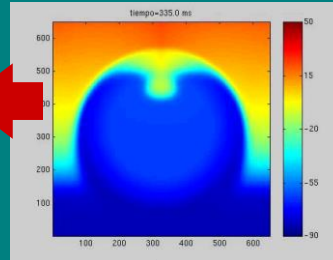
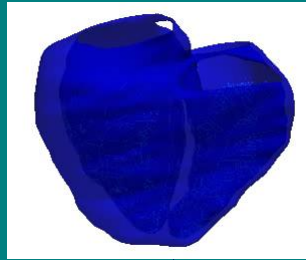
Simulación (corazón infartado, taquicardia ventricular)



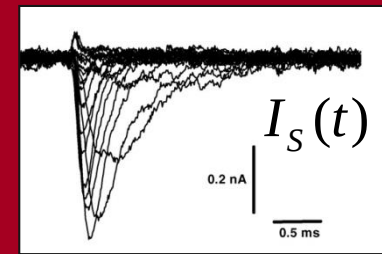
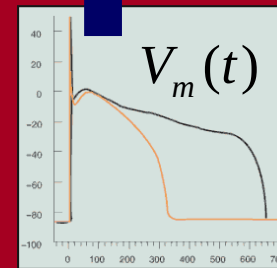
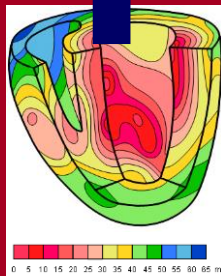
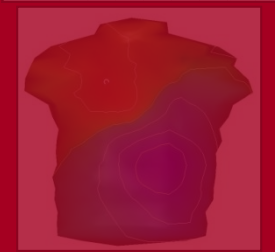
López-Pérez, Sebastián, Izquierdo, Ruiz, Bishop & Ferrero, *Front. In Physiol. (Frontiers in Physiology, 2019)*

Modelado Electrofisiológico Multiescala

Simulación



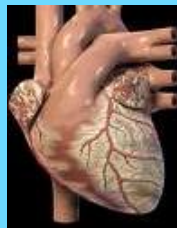
Experimentos



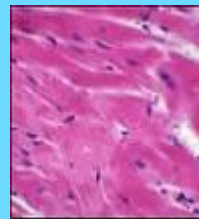
Cuerpo



Órgano



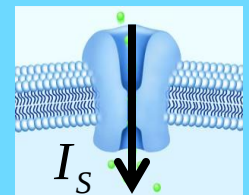
Tejido



Célula



Canal Iónico



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