

**ADVANCES IN  
CARDIAC  
ARRHYTHMIAS**  
*and*  
**GREAT  
INNOVATIONS  
IN CARDIOLOGY**

XXVII Giornate Cardiologiche Torinesi

# What's new in cardiac stem cells

**S. Marra, P. Scacciatella**

*Dipartimento*

*Cardiovascolare e Toracico*

*Città della Salute*

*e della Scienza*

*di Torino*

# CLINICAL NEED

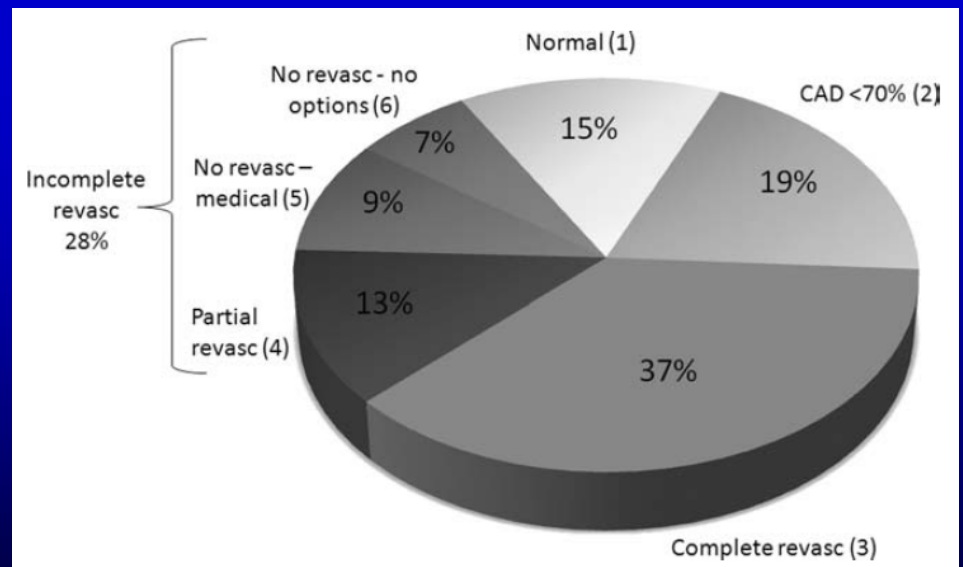
Catheterization and Cardiovascular Interventions 75:886-891 (2010)

## CORONARY ARTERY DISEASE

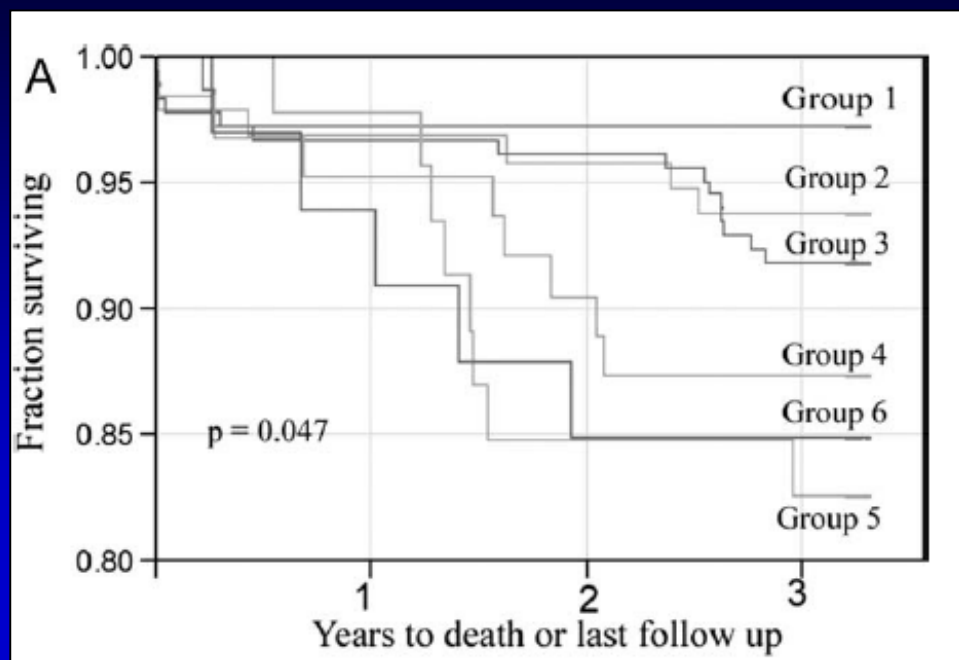
### Original Studies

#### Patients with Coronary Artery Disease Not Amenable to Traditional Revascularization: Prevalence and 3-Year Mortality

Benjamin Williams,<sup>1,2</sup> MD, Madhav Menon,<sup>1,2</sup> MD, Daniel Satran,<sup>1,2</sup> MD, Daniel Hayward,<sup>1</sup> MS, James S. Hodges,<sup>1,3</sup> PhD, M. Nicholas Burke,<sup>1</sup> MD, Randall K. Johnson,<sup>1,2</sup> MD, Anil K. Poulouse,<sup>1</sup> MD, Jay H. Traverse,<sup>1,2</sup> MD, and Timothy D. Henry,<sup>1,2\*</sup> MD



# CLINICAL NEED



**TABLE III. Reasons Precluding Revascularization in Group 6**

Reason for no revascularization <sup>a</sup>	Number	% ( $n = 33$ )
Chronic total occlusion	23	69.7%
Diffuse disease	15	45.5%
Collateral dependent perfusion	14	42.2%
Comorbidities	4	12.1%
Multiple restenoses	2	6.1%
Poor distal targets	1	3.0%

<sup>a</sup>Patients could have more than one reason precluding revascularization.

# CLINICAL NEED



*What's new in cardiac stem cells*

# CLINICAL NEED

Image size: 512 x 512  
View size: 975 x 975  
WL: 138 WW: 189

321/15 ( 65 y , 65 y )  
Cardiac ECO Dose -- EXP 7.5  
R201503201213106  
3

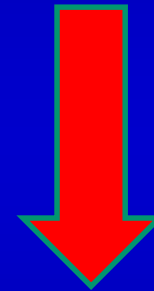


*What's new in cardiac stem cells*

# CLINICAL NEED

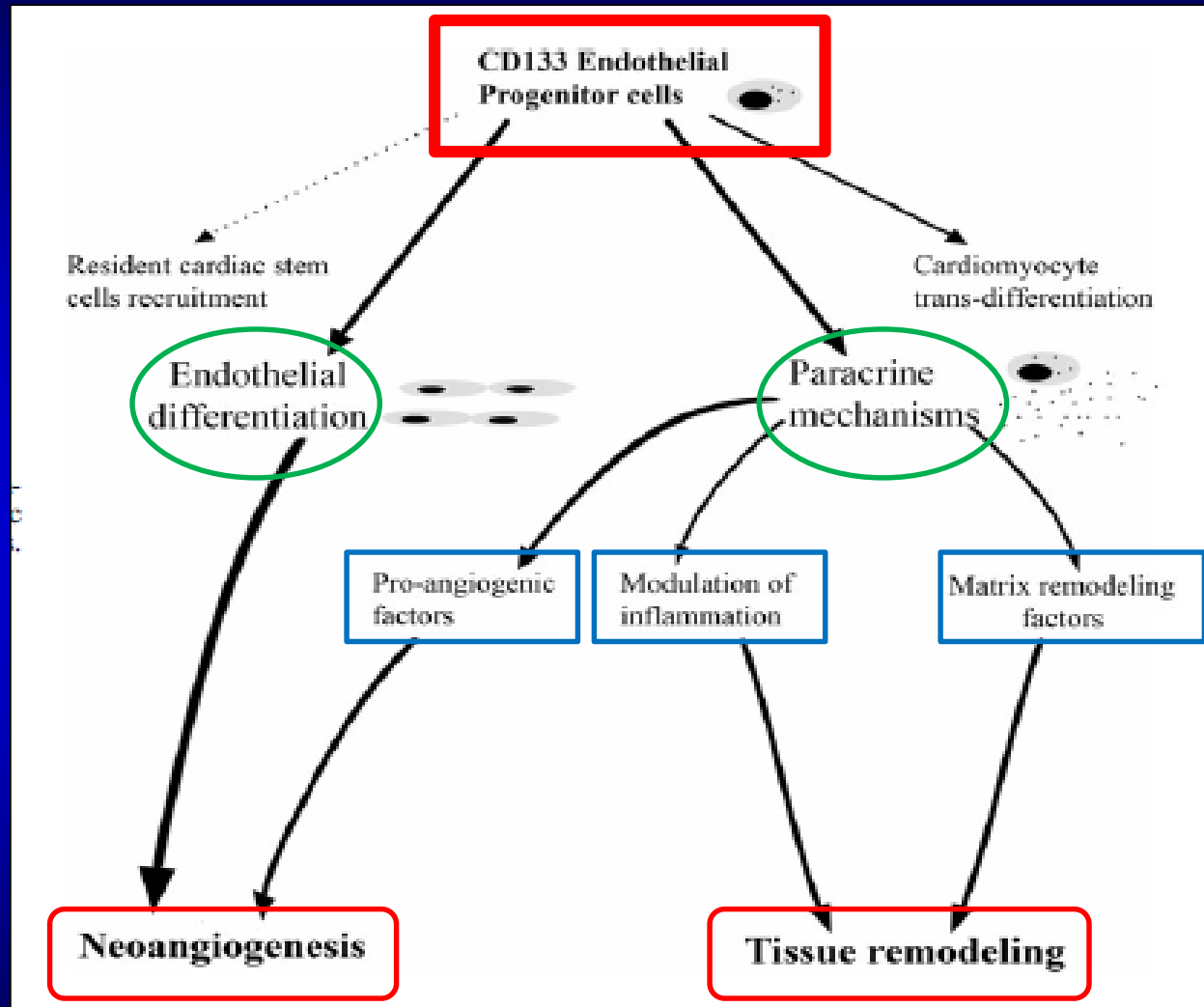


278.710 coronary angio  
in 2013 (GISE data)



9730 NO OPTION patients

# The CD 133 CELL as ADVANCED MEDICINAL PRODUCT for MYOCARDIAL and LIMB ISCHEMIA



Bongiovanni D, Scacciatella P, Pompilio G, et al.  
*Stem Cells and Development* 2014



Centro Cardiologico  
Monzino



**PHASE I TRIAL OF ENDOCAVITARY INJECTION  
OF BONE-MARROW-DERIVED CD133<sup>+</sup> CELLS IN  
ISCHEMIC REFRACTORY CARDIOMYOPATHY  
(RECARDIO trial)**

**Clinicaltrial.gov NCT02059681**

**Eudract: 2012-005267-27**

**Autorizzato da ISS e AIFA il 27/09/2013**



# RECARDIO Trial. Inclusion Criteria

- Heart Failure due to coronary artery disease not amenable to revascularization (surgical or percutaneous)
- NYHA IIb-IV and/or CCS III-IV
- EF 20-45%
- $\text{VO}_2$  max  $\leq$  21 mL/Kg/min
- SPECT LV perfusion reversible defect  $\geq$  10%
- $\geq$  18 e  $\leq$  75 years

# RECARDIO Trial. Criteri di Esclusione

- ACS within 3 months
- LV thrombosis
- Malignant Arrhythmias
- Severe Valvulopathy
- Mechanical Aortic prosthesis
- LV thickness < 8 mm in the target zone
- Previous transplant
- Liver Disfunction (ALT/AST 3 x upper limit)
- Renal Failure (creatinine > 2,5 mg/dL)
- Haemorrhagic disease
- Sepsis
- Infectious disease (HIV, HBV, HCV, VDRL, HTLV1-2)
- Myeloproliferative disorders
- Malignancy within 5 years
- Immunosuppressive therapy
- Pregnancy

# RECARDIO Trial. End point

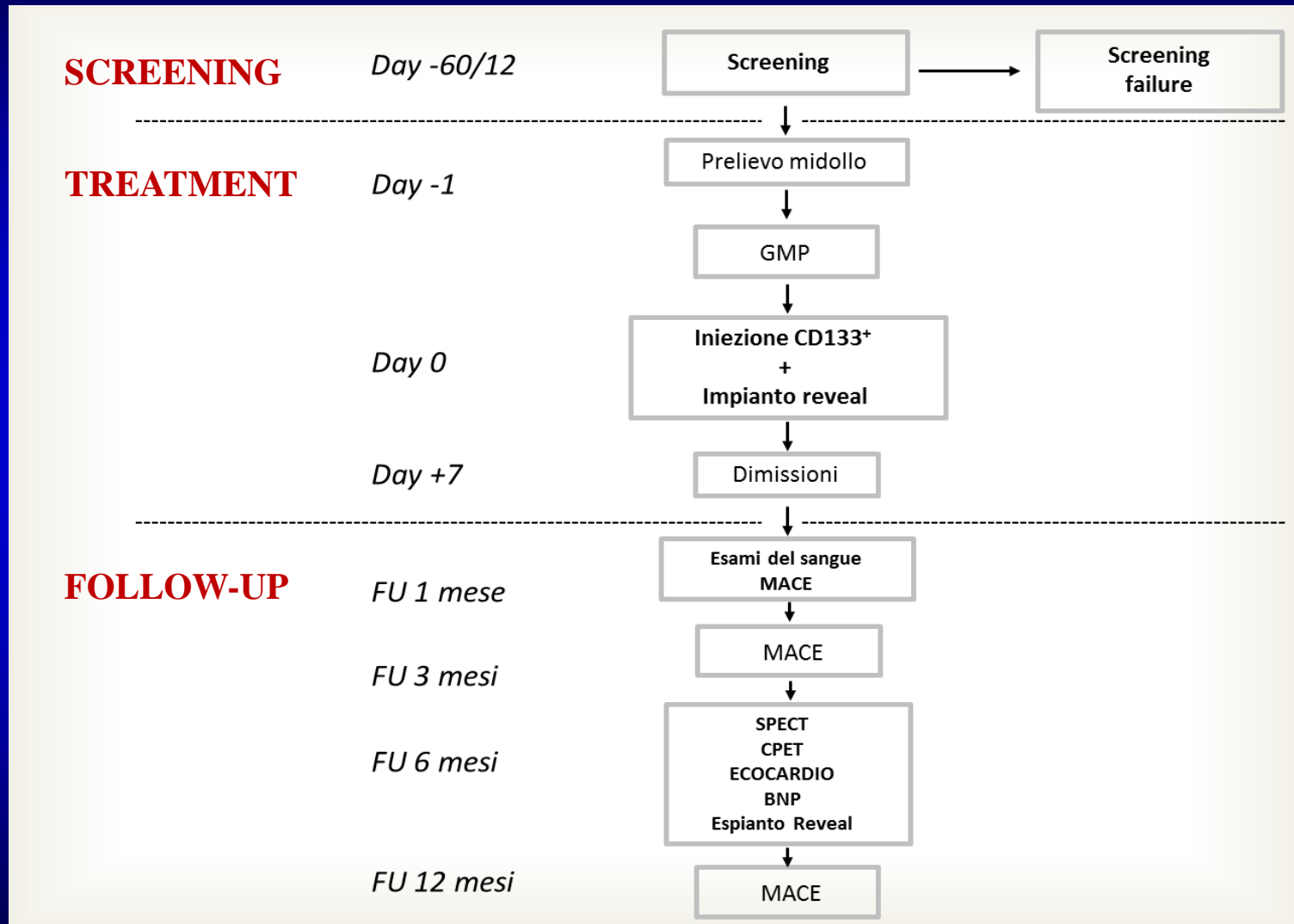
## SAFETY (primary)

- MACE at 12 months:
  - ✓ Death
  - ✓ Myocardial infarction
  - ✓ Heart Failure (hospitalization)
  - ✓ Heart Perforation
  - ✓ Sustained Ventricular Arrhythmias
  - ✓ Ectopic disease

## EFFICACY (secondary)

- SPECT. Target zone perfusion increase (Summed Stress Score, SSS) at 6 months
- VO<sub>2</sub> max increase at 6 months

# RECARDIO Trial. Flow chart



# RECARDIO Trial. Cell Factory

## Cell Therapy LAB "Stefano Verri"



CLASSE B



CLASSE C



CLASSE A

What's new in cardiac stem cells

# RECARDIO Trial. Operations

Torino -  
Milano



Espianto di midollo



San Gerardo-Monza

Midollo osseo

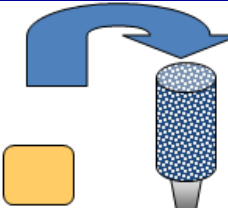


FICOLL

MNCs



+ CD133  
MoAb



Lab Verri -Monza  
(Produzione GMP)

Controlli di qualità:

- conta cellulare
- vitalità cellulare
- immunofenotipo

cellule  
CD133<sup>+</sup>

cellule  
CD133<sup>-</sup>

Controlli di qualità:

- conta cellulare
- vitalità cellulare
- immunofenotipo

Stoccaggio Over-night

Controlli di qualità:

- conta cellulare
- vitalità cellulare
- immunofenotipo
- sterilità
- micoplasma
- endotossina

cellule  
CD133<sup>+</sup>

Torino - Milano  
(uso clinico)



Trasporto (circa 1/2 ore)  
+2-+8°C (Data logger)

# RECARDIO Trial. Helical Infusion System BioCardia

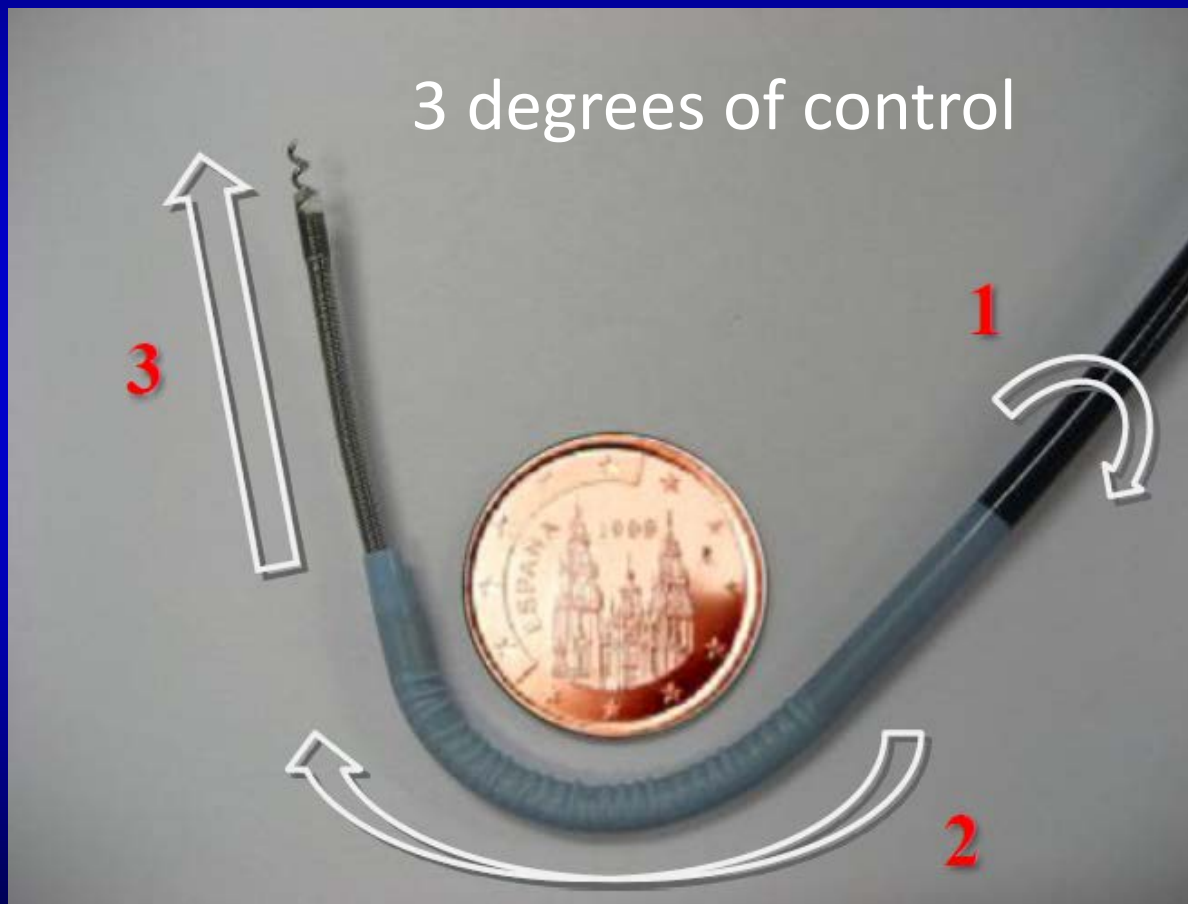
Morph® Universal Deflectable Guide Catheter



Helix Helical Infusion Catheter



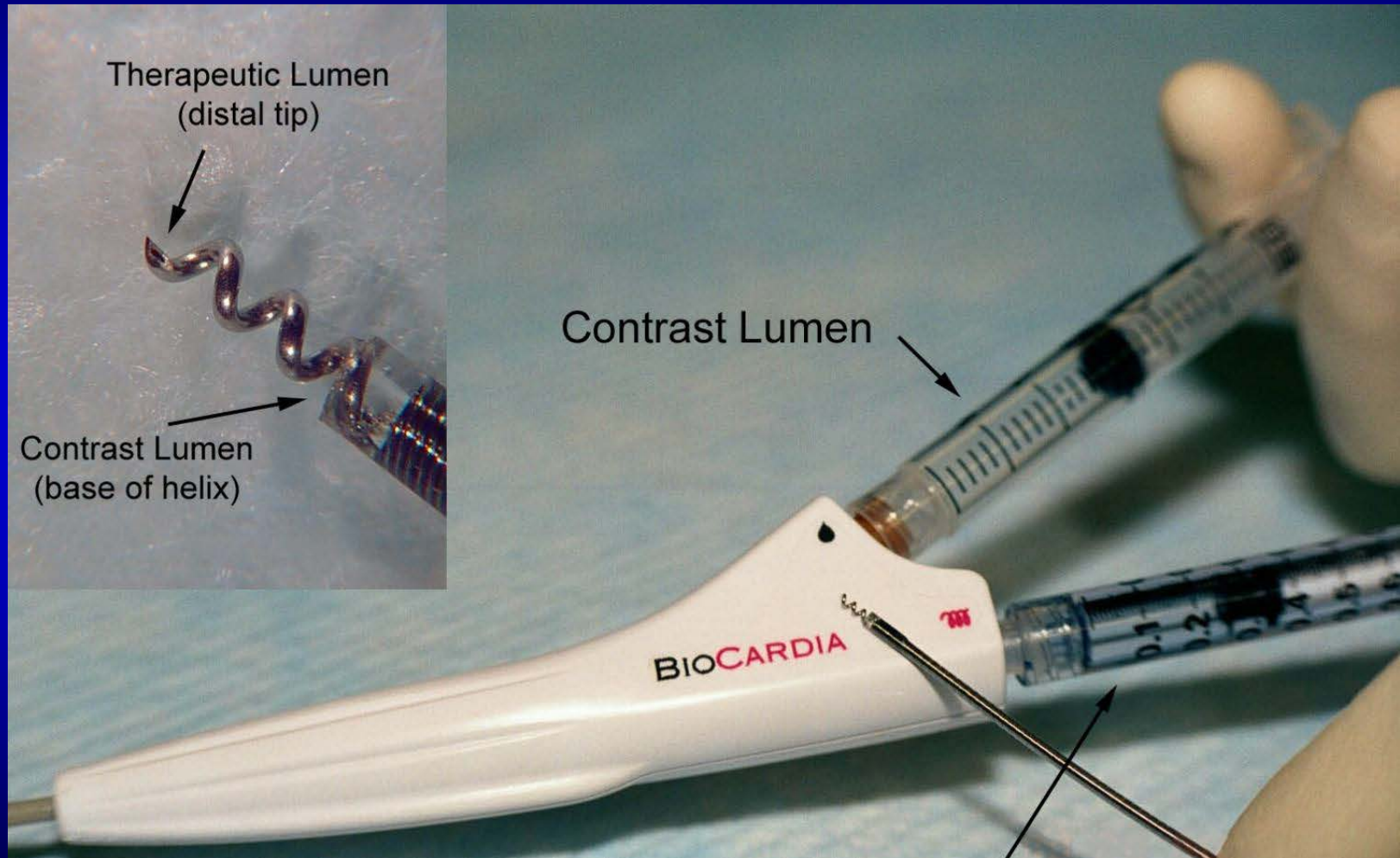
# RECARDIO Trial. Helical Infusion System BioCardia



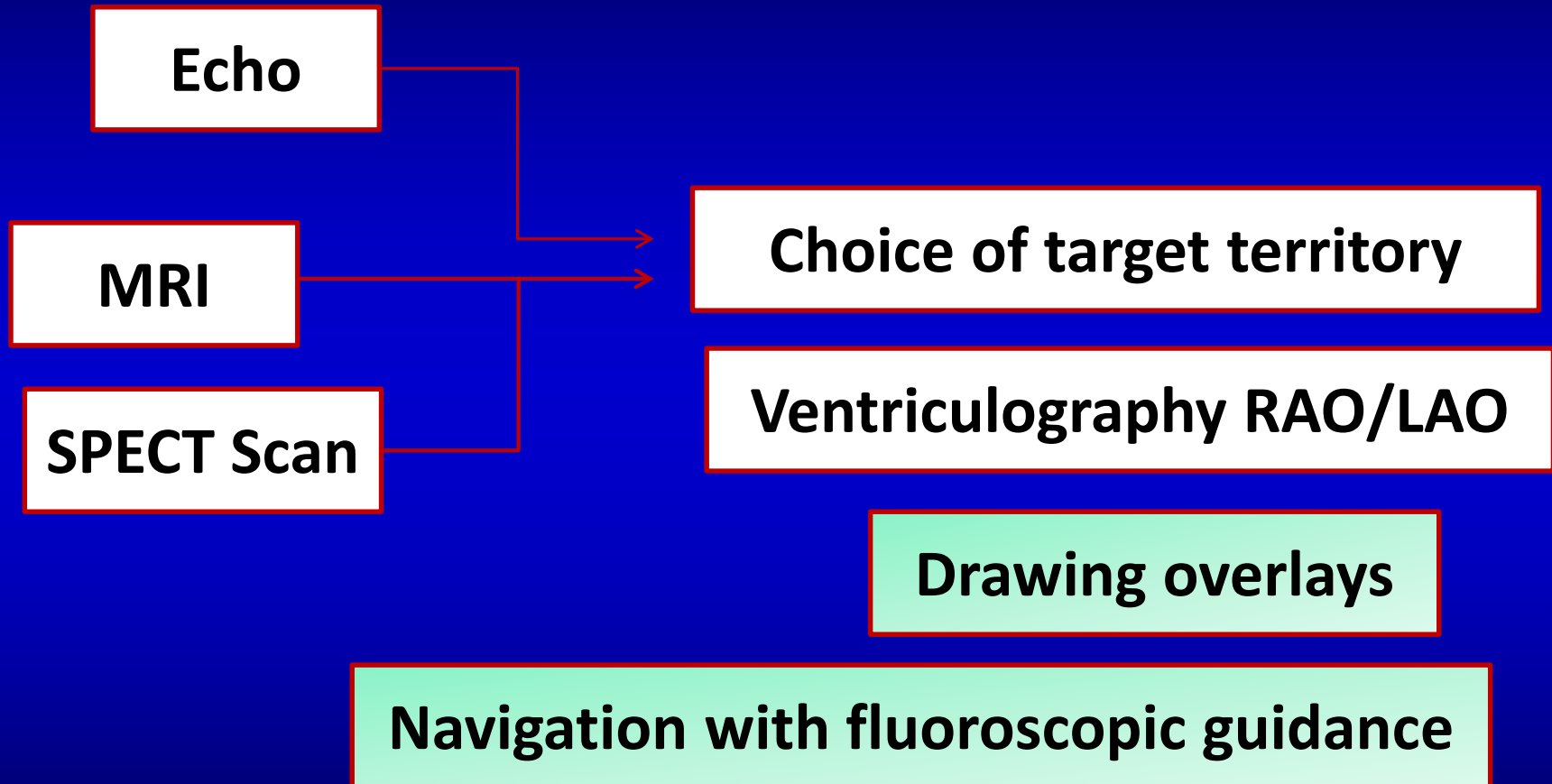


# RECARDIO Trial.

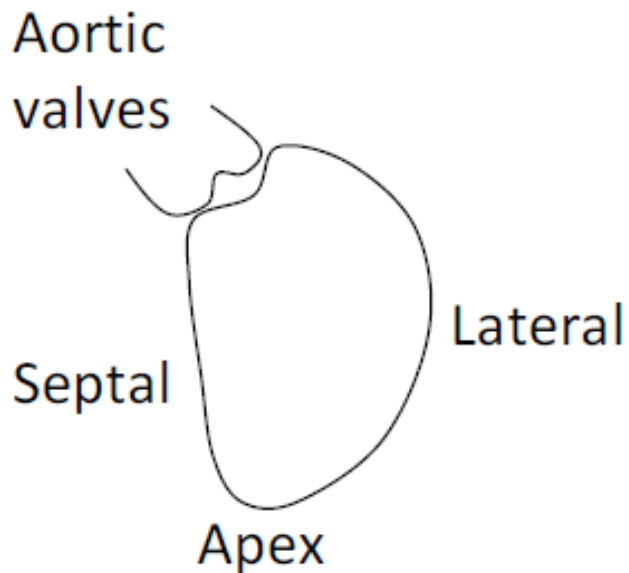
## Helical Infusion System BioCardia



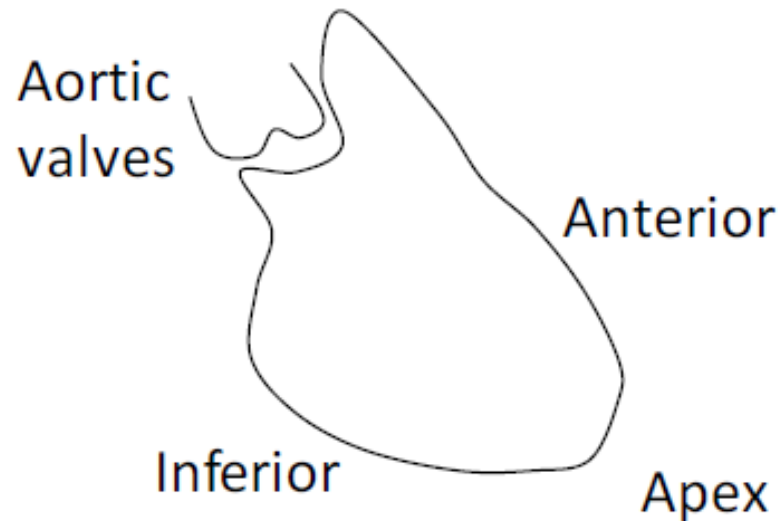
# RECARDIO Trial. Cells Implantation. Target zone.



# RECARDIO Trial. Cells Implantation. Target zone.



**Left Anterior Oblique (LAO)**



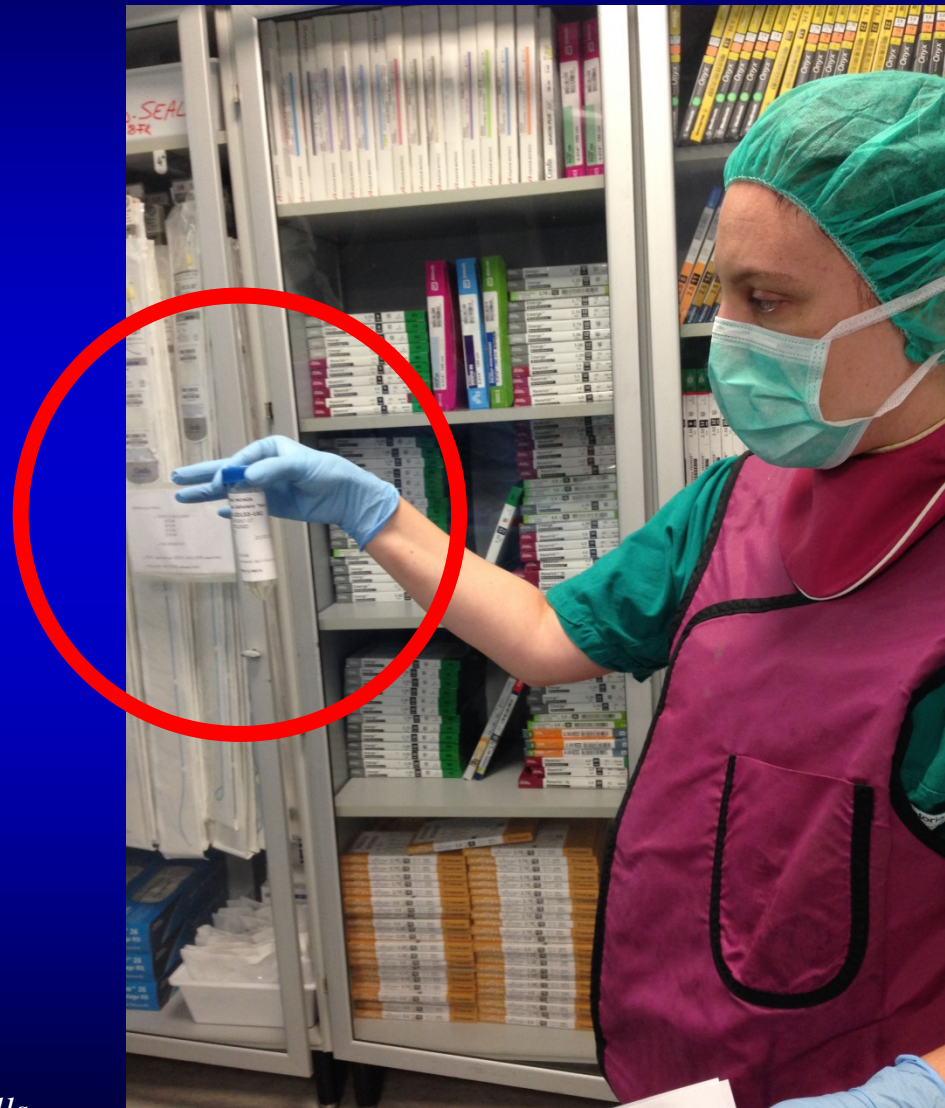
**Right Anterior Oblique (RAO)**

**RECARDIO Trial. 2/7/2015. 1° caso**  
**Città della Salute e della Scienza di Torino**



*What's new in cardiac stem cells*

**RECARDIO Trial. 2/7/2015. 1° caso**  
**Città della Salute e della Scienza di Torino**



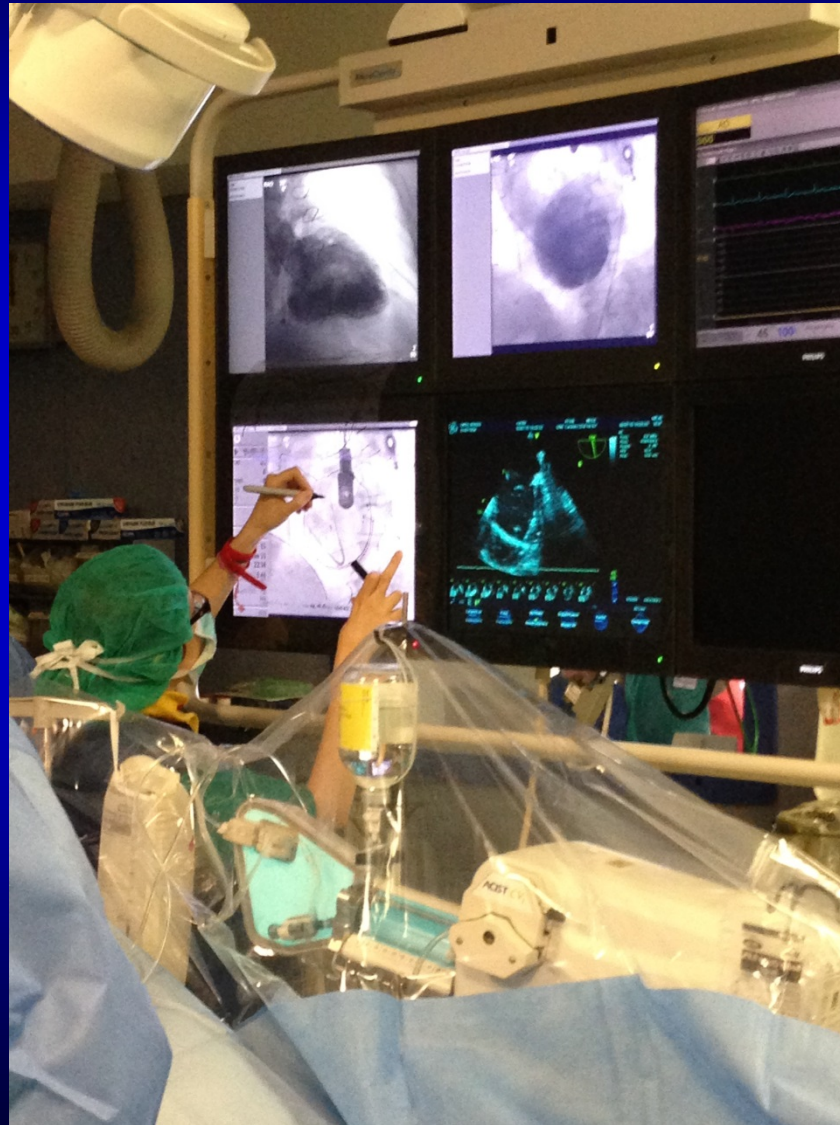
*What's new in cardiac stem cells*

**RECARDIO Trial. 2/7/2015. 1° caso**  
**Città della Salute e della Scienza di Torino**



*What's new in cardiac stem cells*

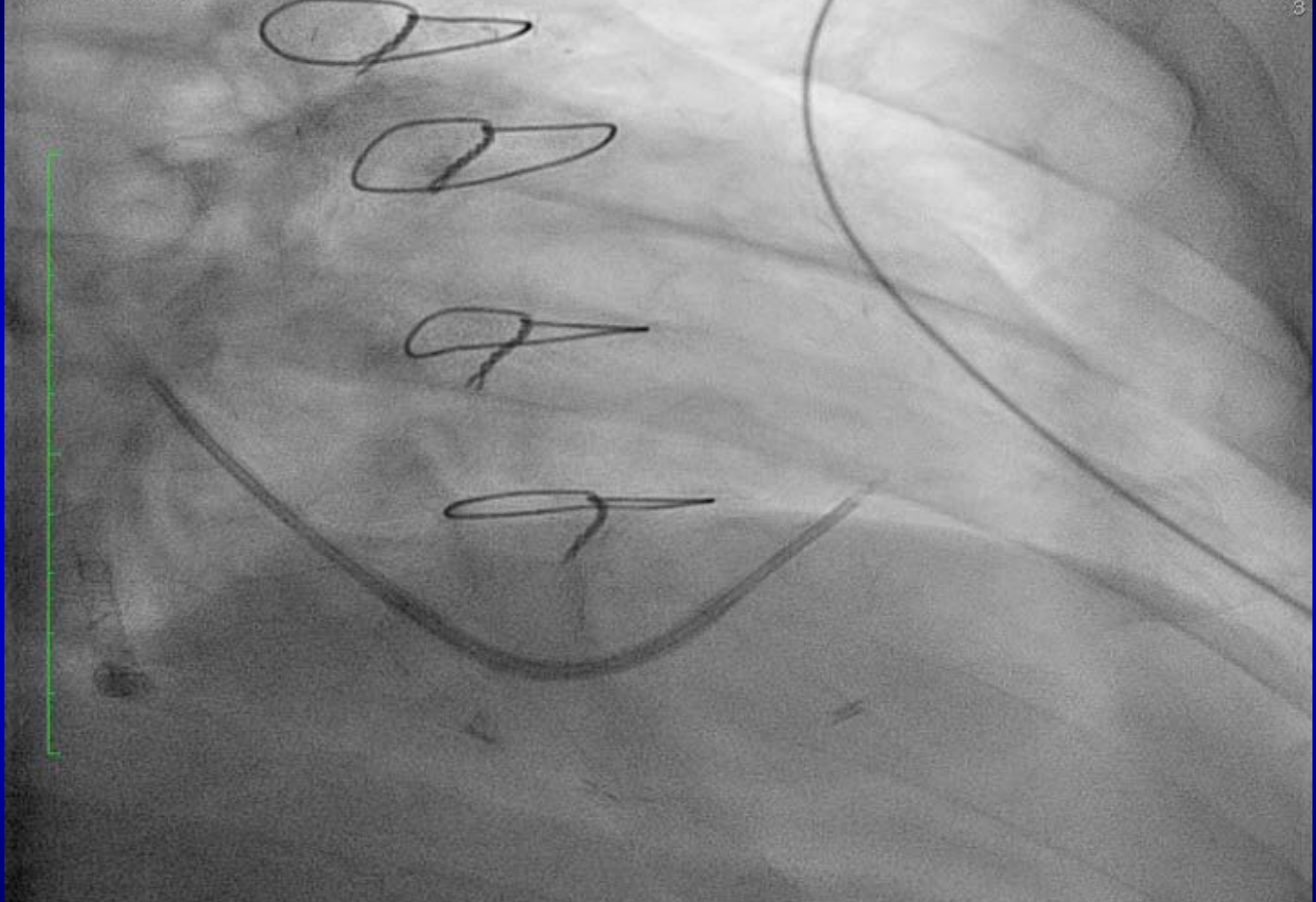
**RECARDIO Trial. 2/7/2015. 1° caso**  
**Città della Salute e della Scienza di Torino**



*What's new in cardiac stem cells*

Image size: 512 x 512  
View size: 975 x 975  
Wt.: 129 WW: 150

708 ( 65 y , 65 y )  
Cardiac Clarity 15 fps -- L.Coro 15 fpsNorm  
R201507021218008  
3



Zoom: 190% Angle: 0  
Im: 1/68  
Uncompressed

02/07/15 14:21:19  
Made In OsiriX

*What's new in cardiac stem cells*



Image size: 512 x 512  
View size: 975 x 975  
WL: 129 WW: 150

708 ( 65 y , 65 y )  
Cardiac Clarity15 fps -- L:Coro 15 fpsNorm  
R201507021218008  
4

Zoom: 190% Angle: 0  
Im: 1/66  
Uncompressed

02/07/15 14:29:32  
Made In OsiriX

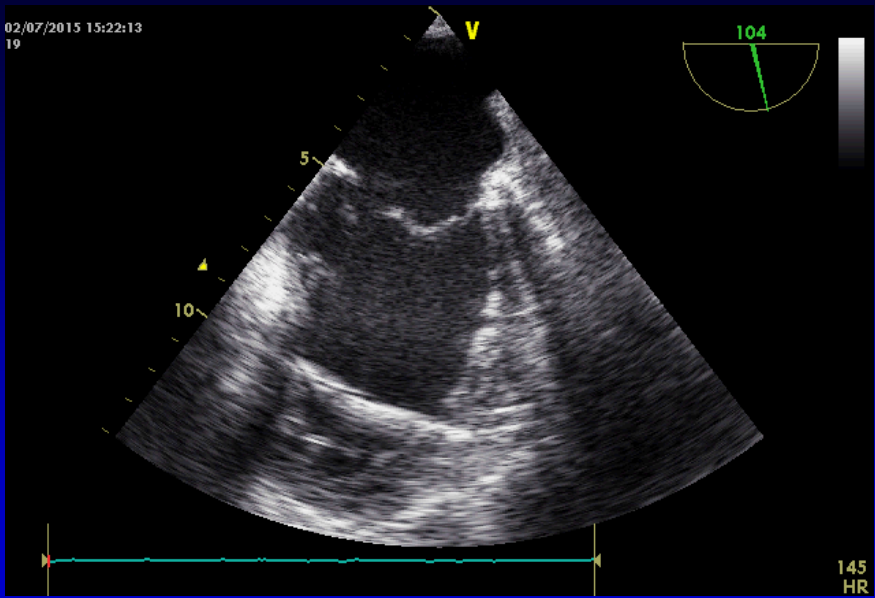
708 ( 65 y , 65 y )  
Cardiac Clarity15 fps -- L:Coro 15 fpsNorm  
R201507021218008  
5

Zoom: 190% Angle: 0  
Im: 1/73  
Uncompressed

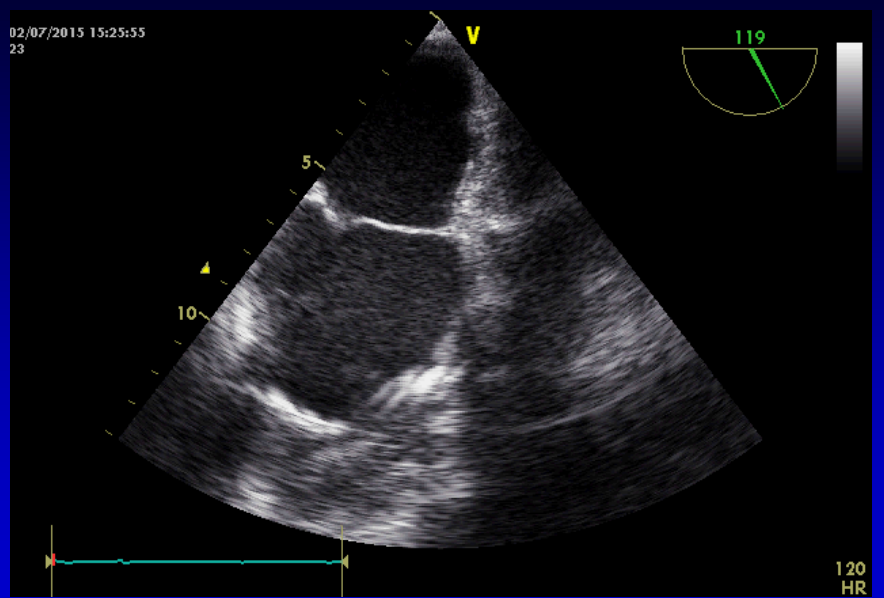
02/07/15 14:34:24  
Made In OsiriX

*What's new in cardiac stem cells*

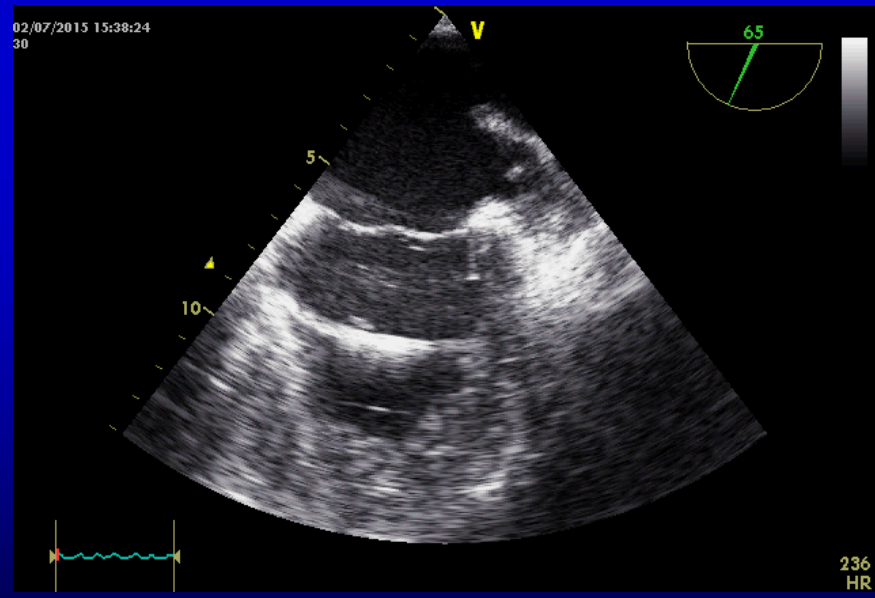
02/07/2015 15:22:13  
19



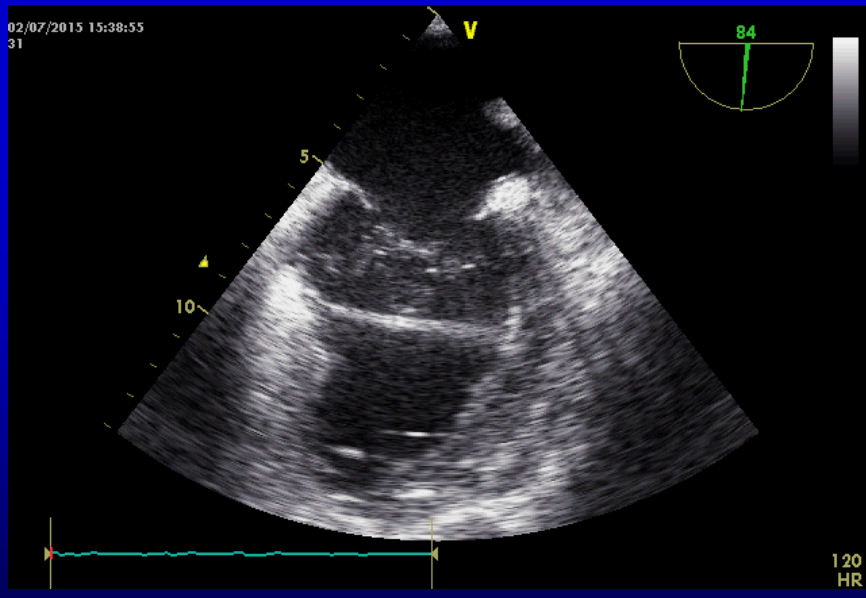
02/07/2015 15:25:55  
23



02/07/2015 15:38:24  
30

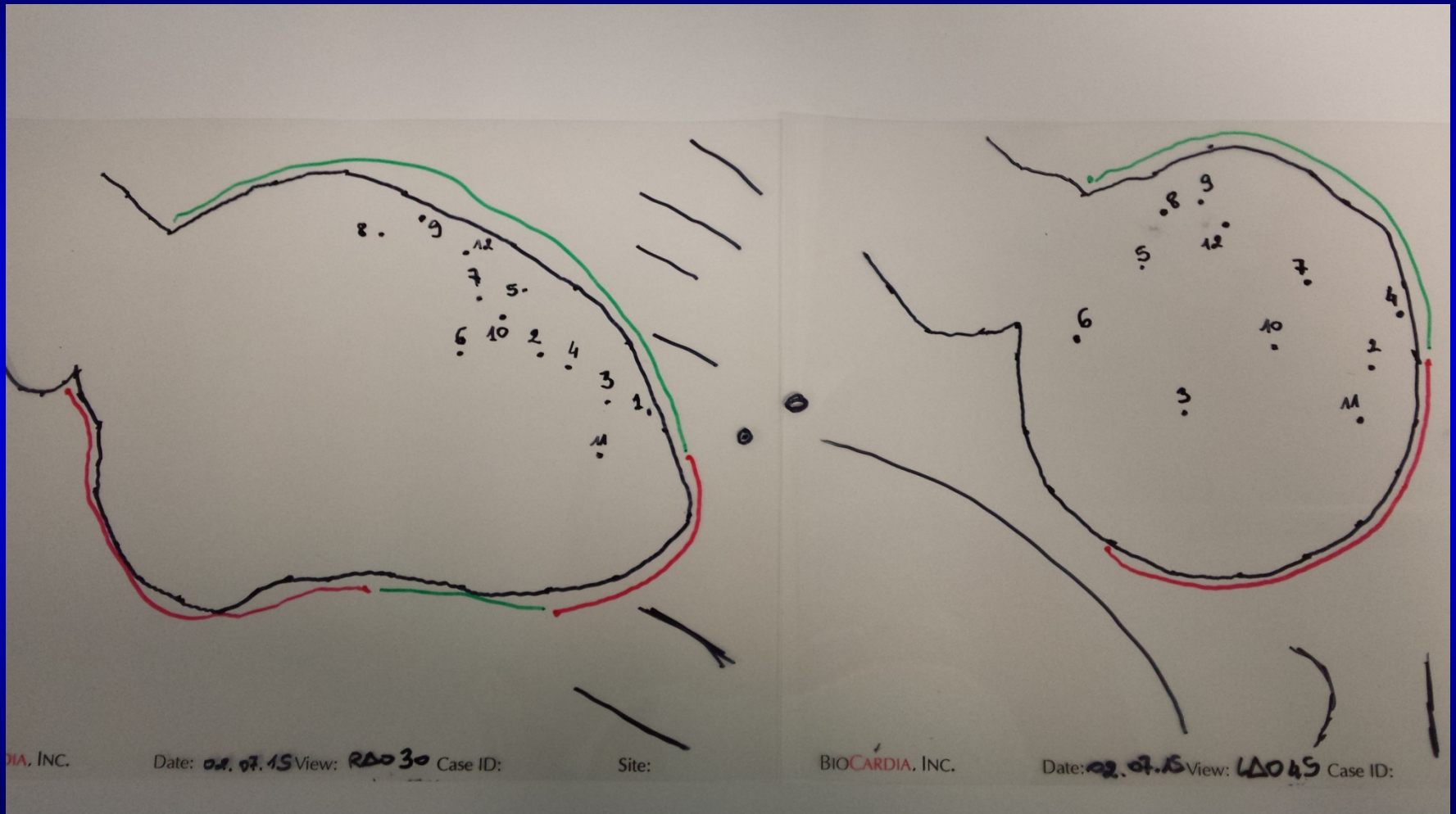


02/07/2015 15:38:55  
31



*What's new in cardiac stem cells*

# RECARDIO Trial. 2/7/2015. 1° caso Città della Salute e della Scienza di Torino



# RECARDIO Trial. 2/7/2015. 1° caso Città della Salute e della Scienza di Torino



*What's new in cardiac stem cells*

# RECARDIO Trial. Preliminary Data

7 pts enrolled and treated

NO procedural MACE

NO events during follow up

# RECARDIO Trial. Preliminary Data

Paziente 1-001

PRE-OP

POST-OP

**Canadian Class**

III

II

**NYHA**

III/IV

II

**Nitrati**

1/die

1/mese

**Test cardiopolmonare da sforzo**

12,5

16

**SSS**

13

7

**FE %**

41,8

44,5

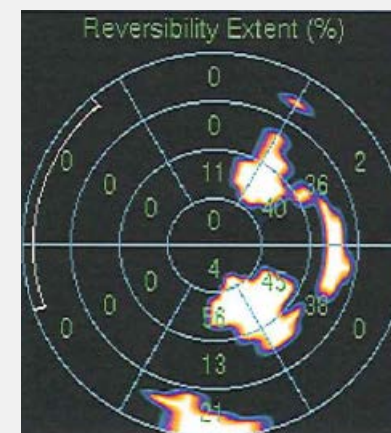
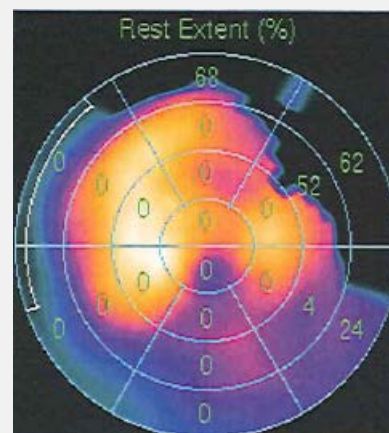
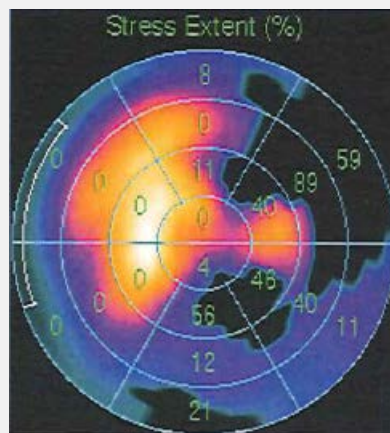
**BNP**

530

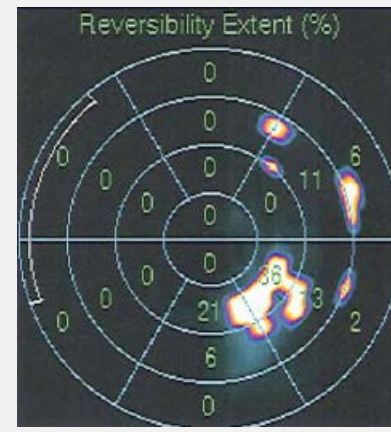
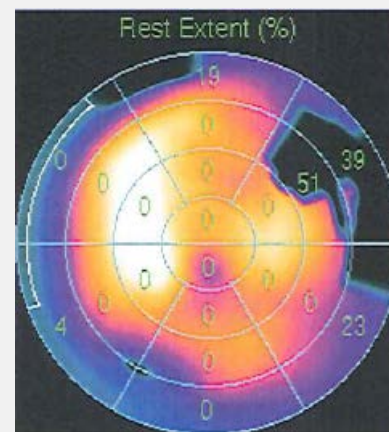
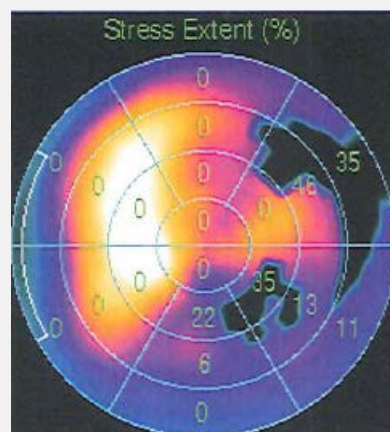
568

# RECARDIO Trial. Preliminary Data

Pre-op



Post-op



# Amici del Cuore®

PIEMONTE ONLUS

Associazione di volontariato per la  
prevenzione delle malattie cardiovascolari

*«...Generoso supporto alla ricerca scientifica...»*



## **Grazie dell'attenzione**

### ***Principal Investigator***

Prof. Giulio Pompilio

### ***Co-investigators***

Dott. Sebastiano Marra

Prof. Fiorenzo Gaita

Dott. Paolo Scacciatella

Dott. Felice Achilli

Dott. Corrado Carbucicchio

### ***Study Coordinator***

Dott. Beatrice Bassetti

### ***Investigators Città della Salute e della Scienza di Torino***

Prof. Benedetto Bruno (ematologia)

Dott. Massimo Baccega (SPECT)

Dott. Monica Andriani (RM, SPECT)

Dott. Serena Beninati (Clinics)

Dott. Carlo Budano (loop recorder)

Dott. Luca Checco (CP test)

Dott. Mauro Giorgi (Echo)

Coord. Inf. Anella Rizzo (coordinamento gestionale)

Inf. Antonello Carmeci (nursing)

Dott. Lorenza Michela Biava (data manager)