

# Terapia Gênica em Cardiologia

# Terapia Gênica para Angina Refratária: Estado Atual e Resultados de um Ensaio Clínico Brasileiro.



Apoio:  
FAPERGS, FINEP, FAPICC, CNPq, FUC/RS

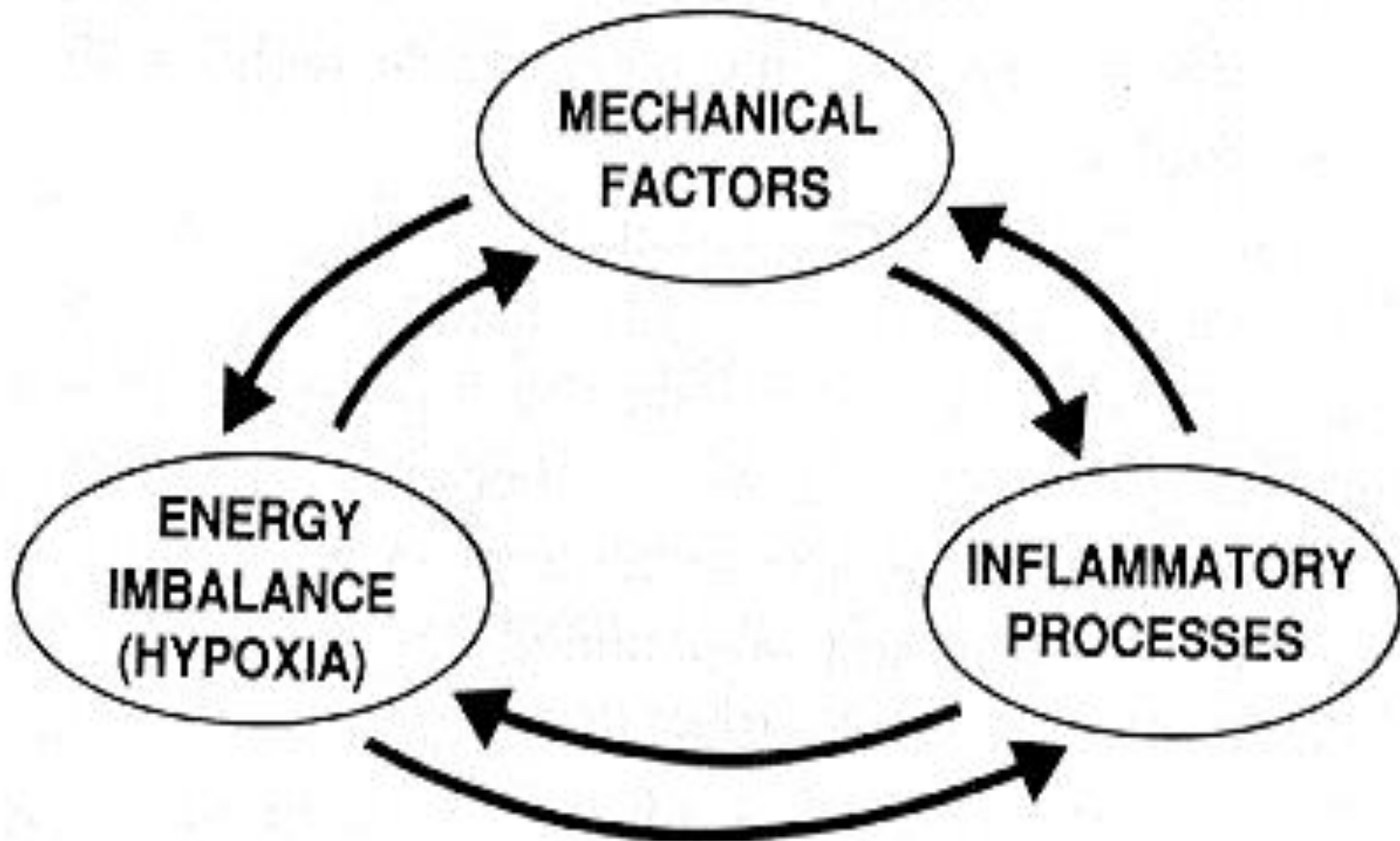


# Angina Refratária

- 6.600.000 casos de Angina diagnosticados nos EUA
- Cardiopatia isquêmica sintomática sem possibilidade de tratamento cirúrgico ou percutâneo;
- ↓ mortalidade por DAC    ↑ incidência de angina refratária.
- Até 11,8% dos pacientes que realizam cinecoronariografia em hospital terciário não são passíveis de tratamento intervencionista
- Alto risco: 25.5% de IAM e 19.9 % de morte em 1 ano

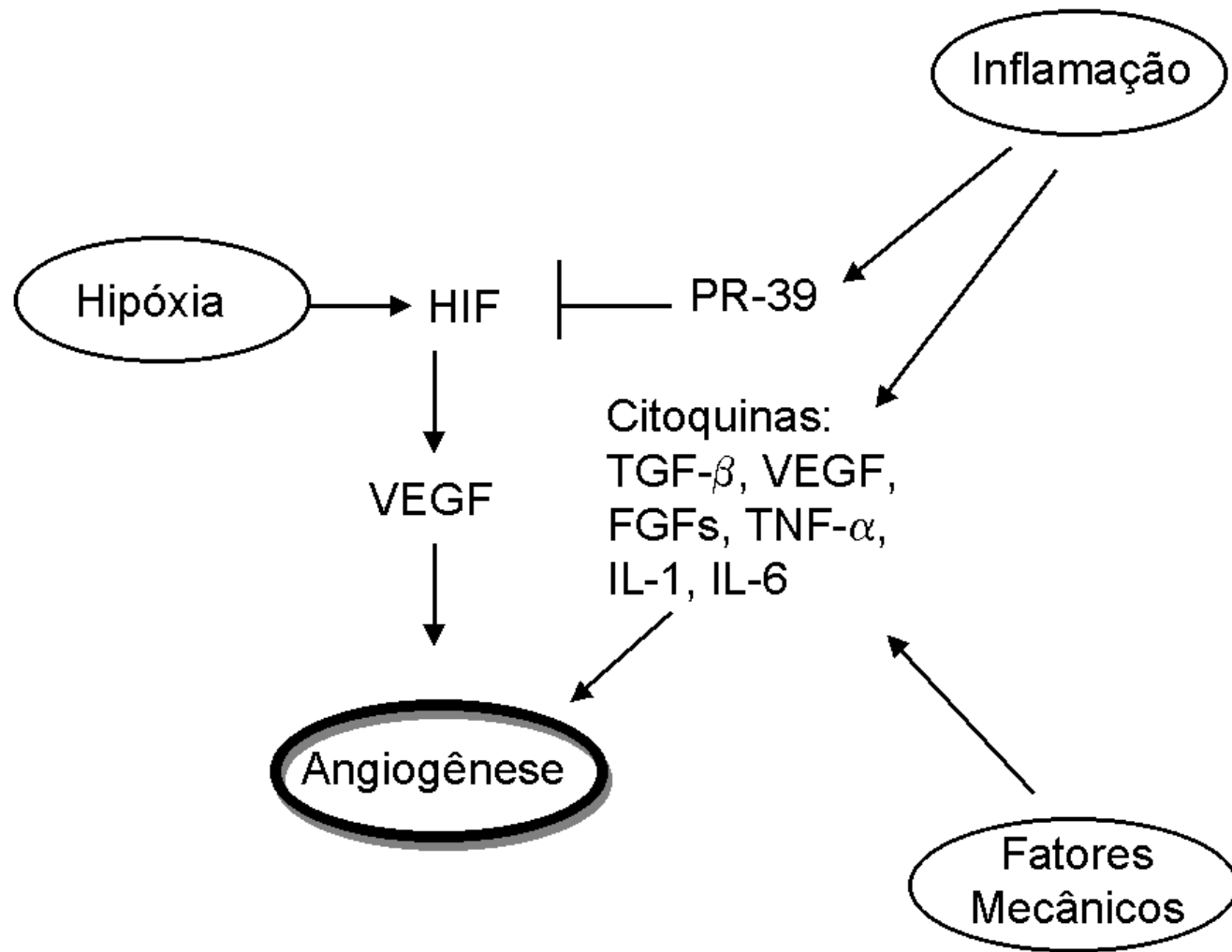
# Tratamento da angina refratária

- Farmacológico
- Mecânico: Contrapulsção externa aumentada, laser, estimulação da medula espinhal
- Angiogênese terapêutica:
  - Uso de proteínas recombinantes
  - Terapia gênica
  - Terapia celular



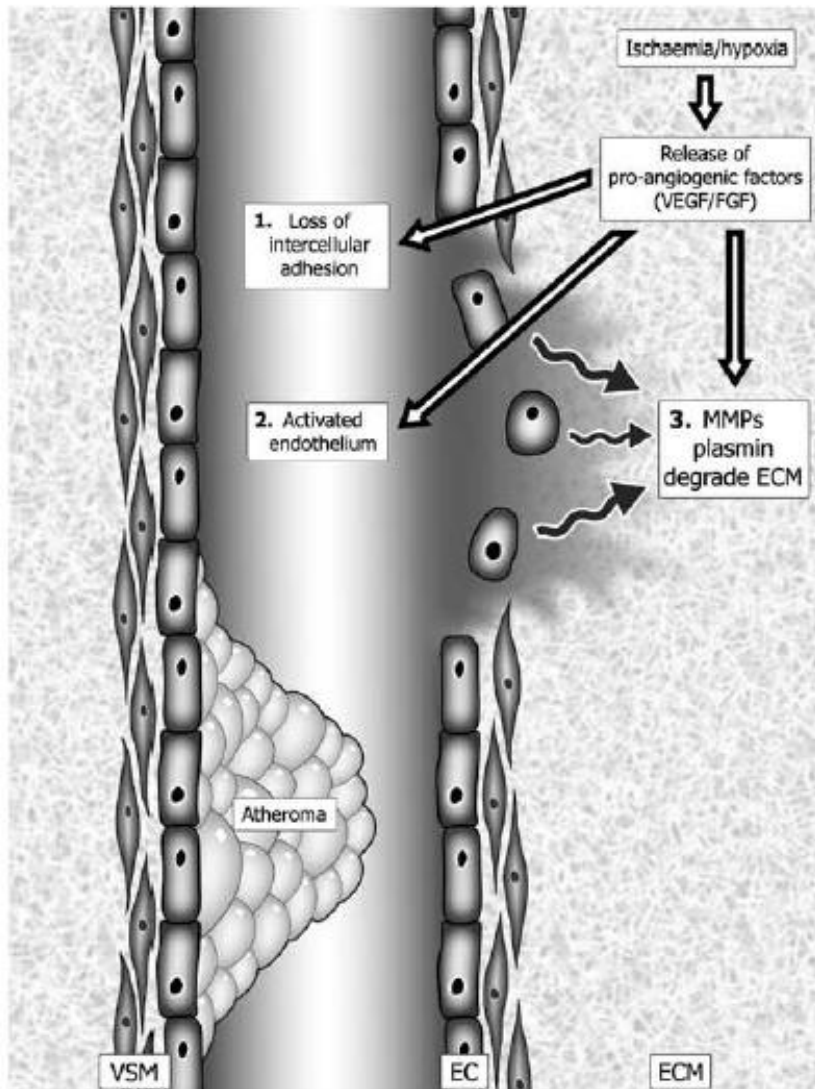
Major factors leading to the initiation of angiogenesis.

# Fatores determinantes e mediadores de angiogênese

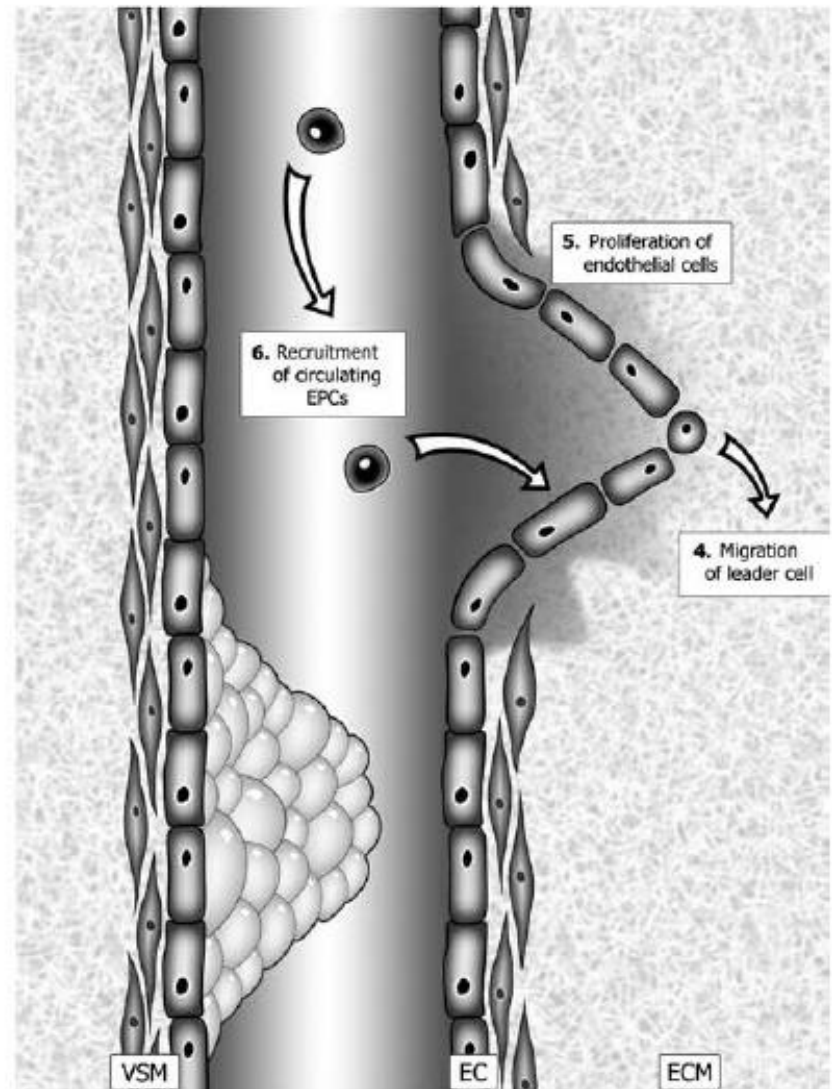


# Angiogenesis

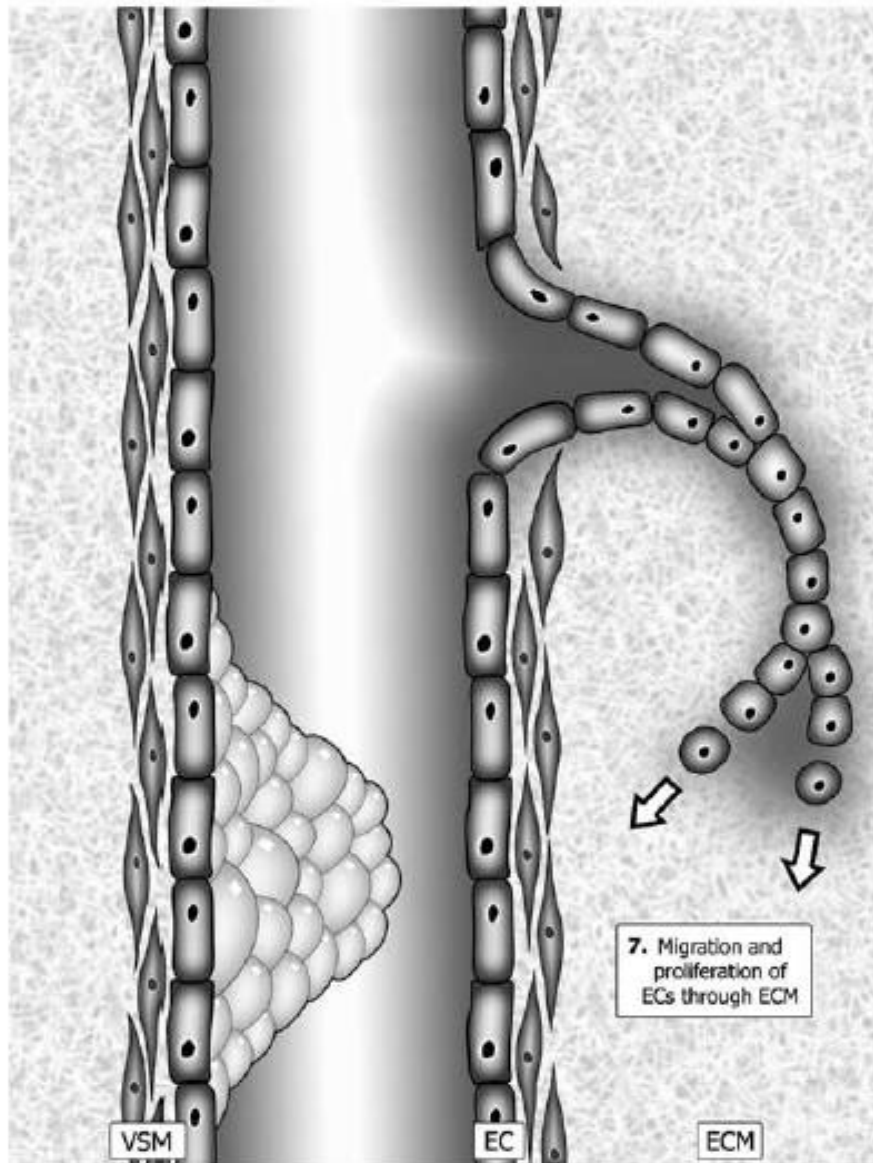
**A.**



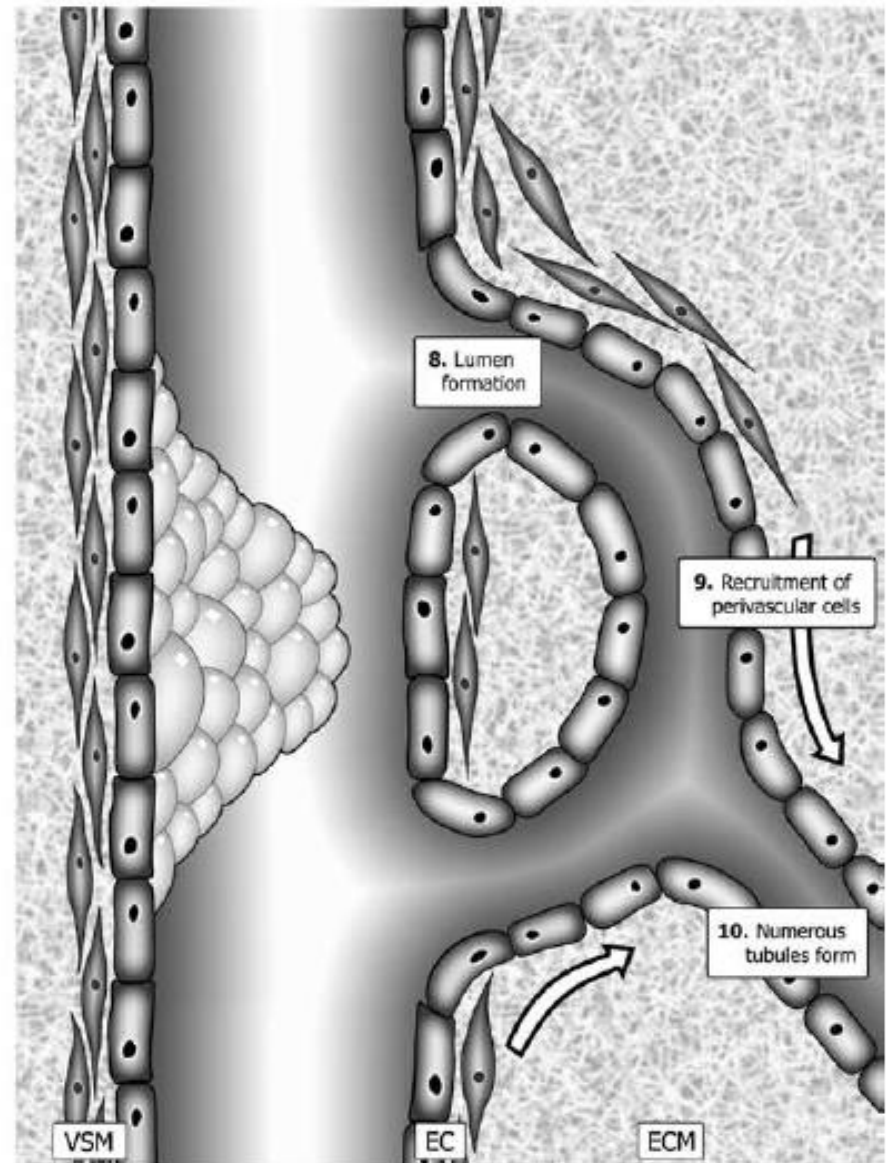
**B.**



**C.**

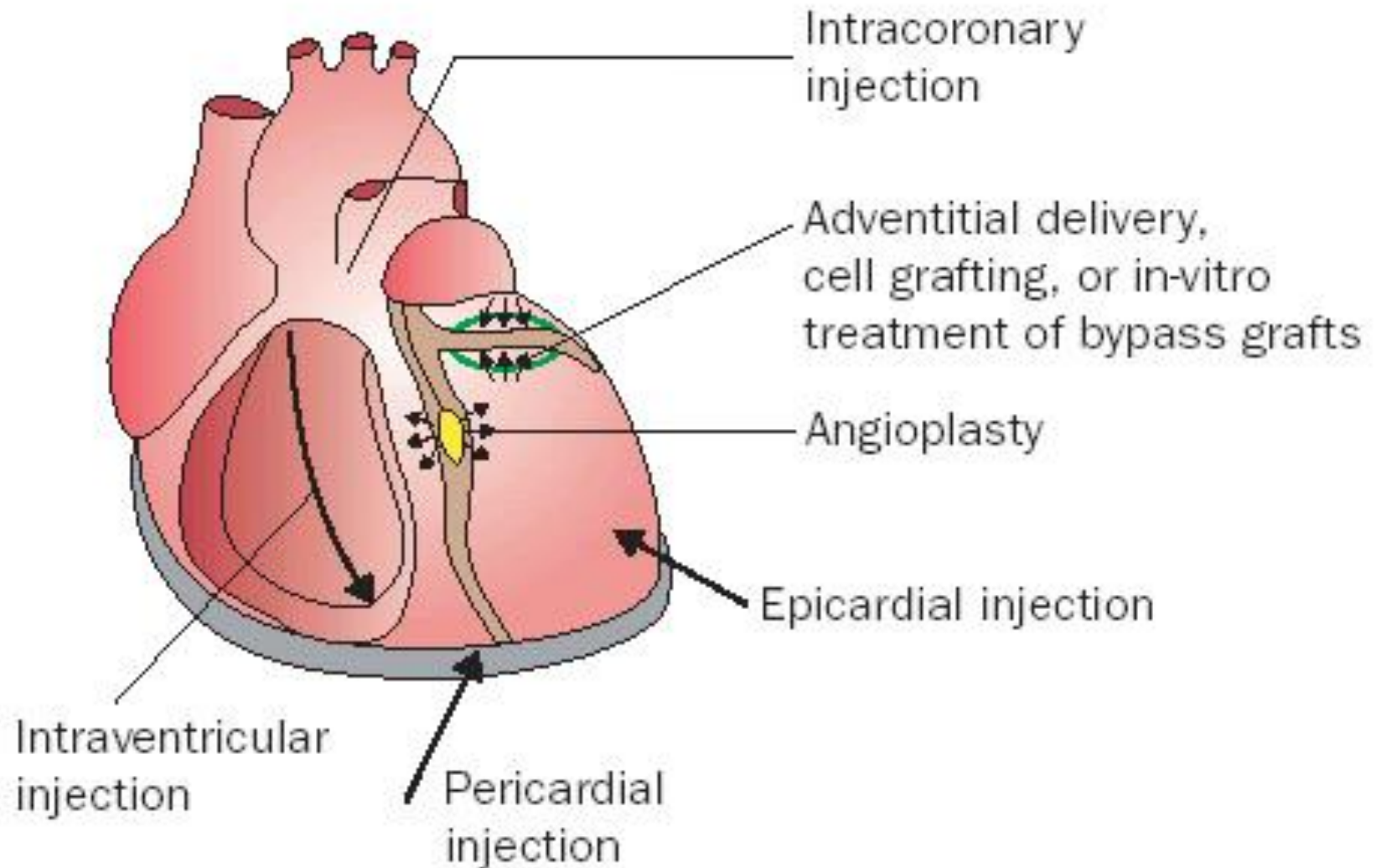


**D.**

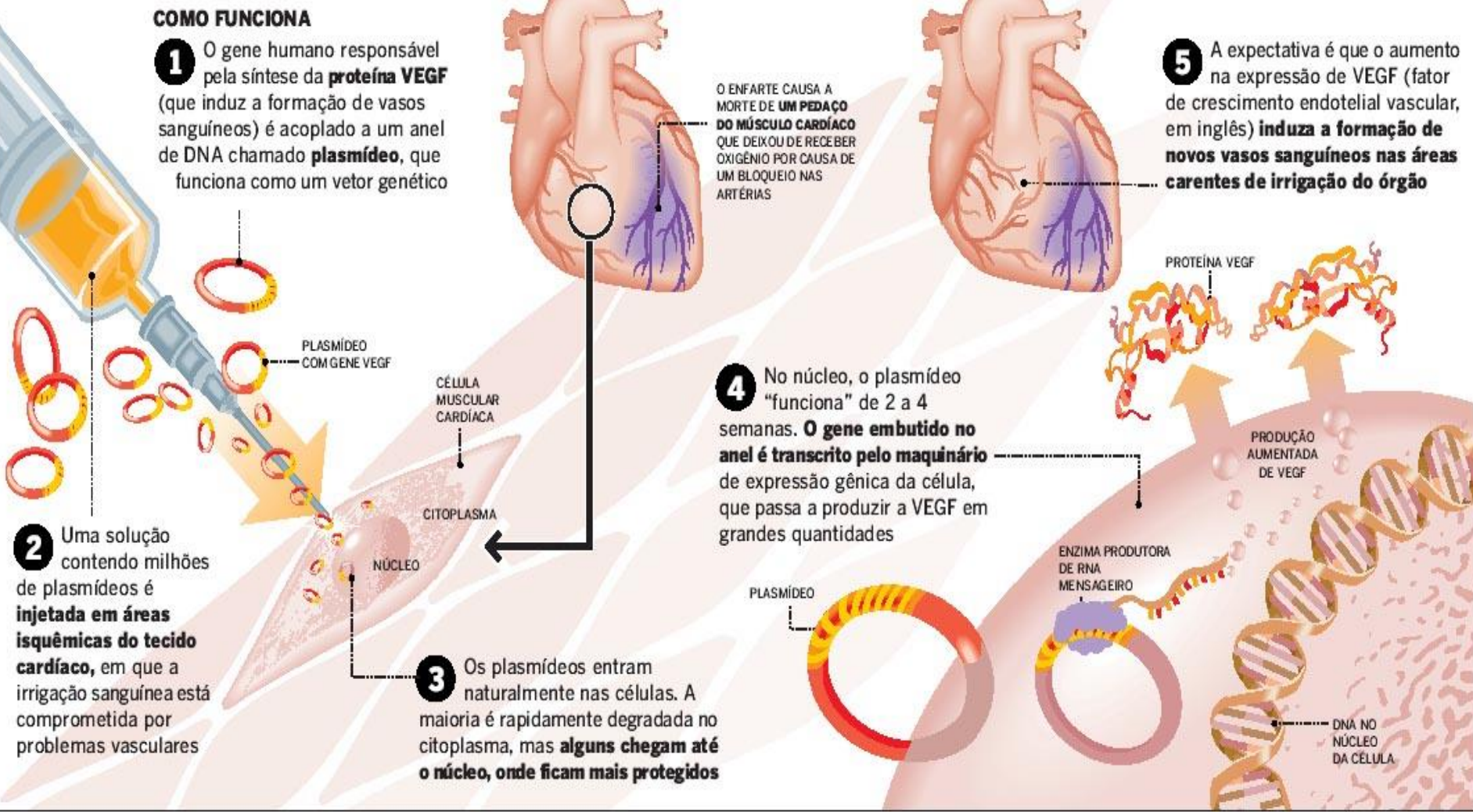




Seppo Y, Martin JF. The Lancet 355:213-222,2000

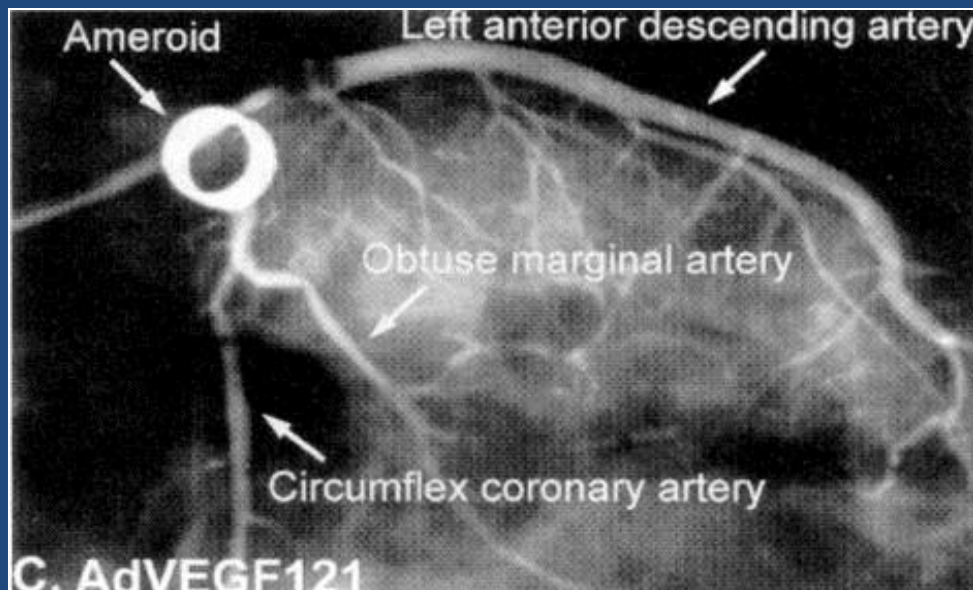
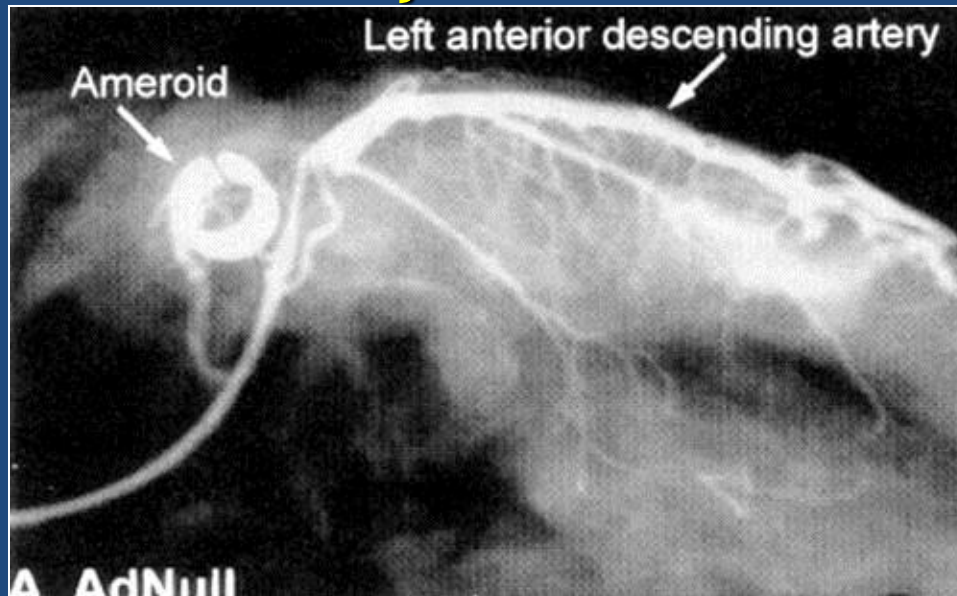


O primeiro teste clínico com terapia gênica no Brasil, em andamento no Rio Grande do Sul, busca induzir a revascularização de áreas isquêmicas do coração



# Terapia Angiogênica por Vetor Viral Ad – VEGF<sub>121</sub>

## Via Administração: Intramiocárdica

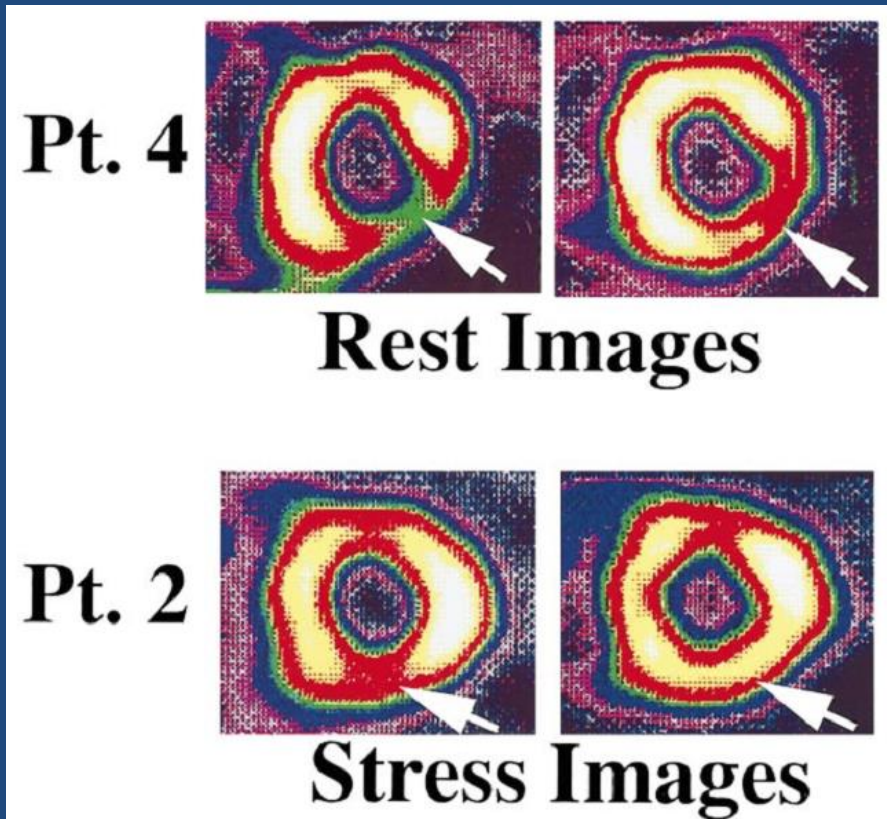
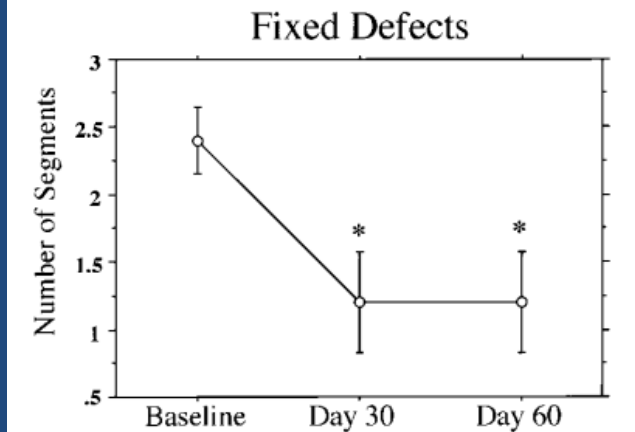
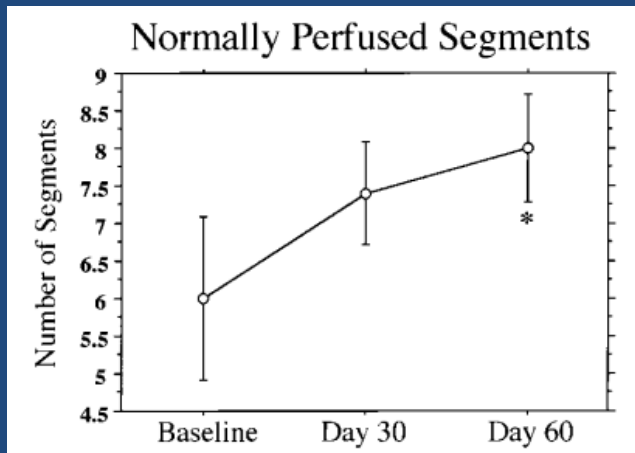


# Gene Therapy for Myocardial Angiogenesis : Initial Clinical Results With Direct Myocardial Injection of phVEGF 165 as Sole Therapy for Myocardial Ischemia

Douglas W. Losordo, Peter R. Vale, James F. Symes, Cheryl H. Dunnington, Darryl D. Esakof, Michael Maysky, Alan B. Ashare, Kishor Lathi and Jeffrey M. Isner  
*Circulation* 1998;98;2800-2804

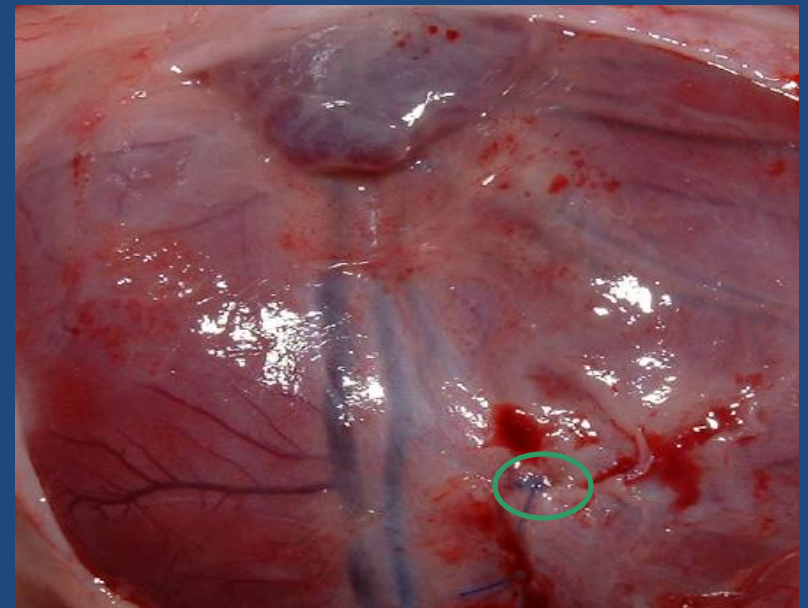
**Background**—We initiated a phase 1 clinical study to determine the safety and bioactivity of direct myocardial gene transfer of vascular endothelial growth factor (VEGF) as sole therapy for patients with symptomatic myocardial ischemia.

**Método:**  $n=5$  pacientes 125  $\mu\text{g}$  VEGF 165 via intramiocárdica direta

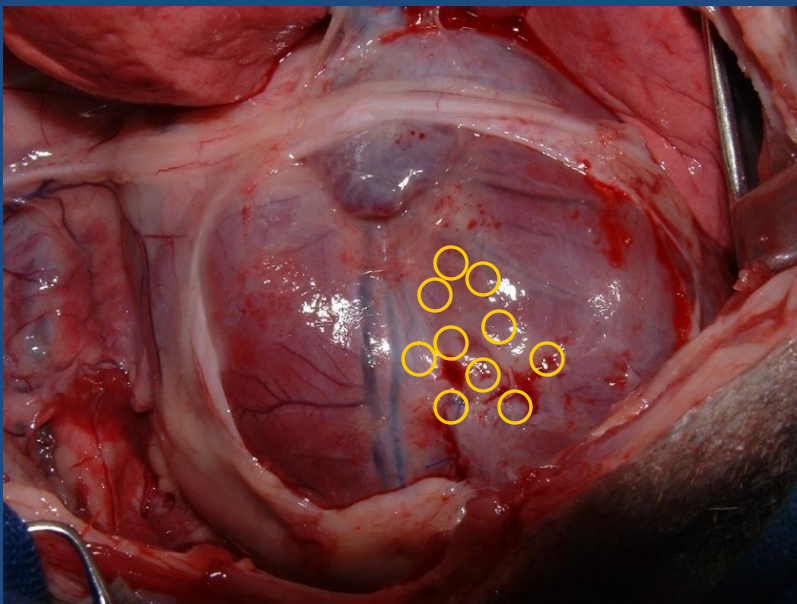




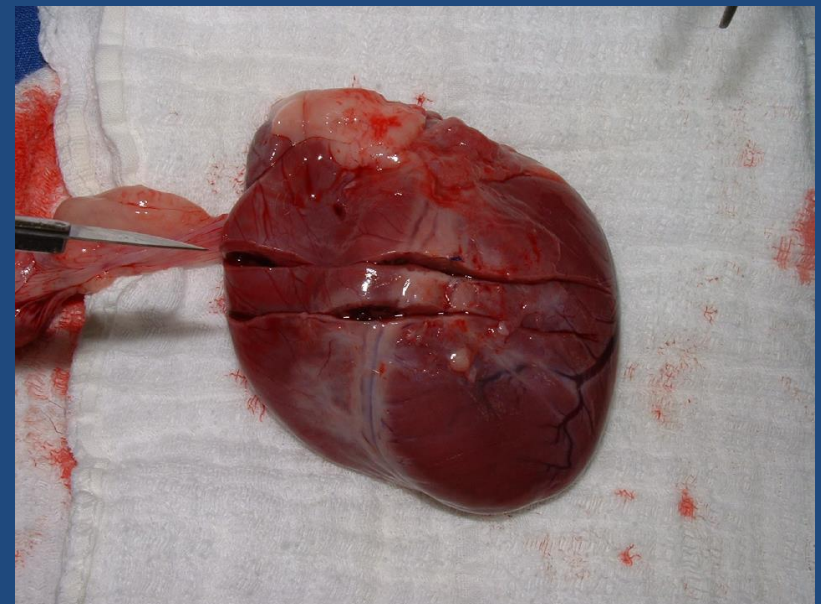
Incisão



Ligadura da coronária



Pontos de injeção



Preparação para histologia

# Angiogênese por Terapia Gênica

## Estudo Experimental IC-FUC

VEGF<sub>165</sub> (plasmídeo)

**Genentech, Inc.**

1 DNA Way

South San Francisco, CA 94080-4990

(650) 225-1000

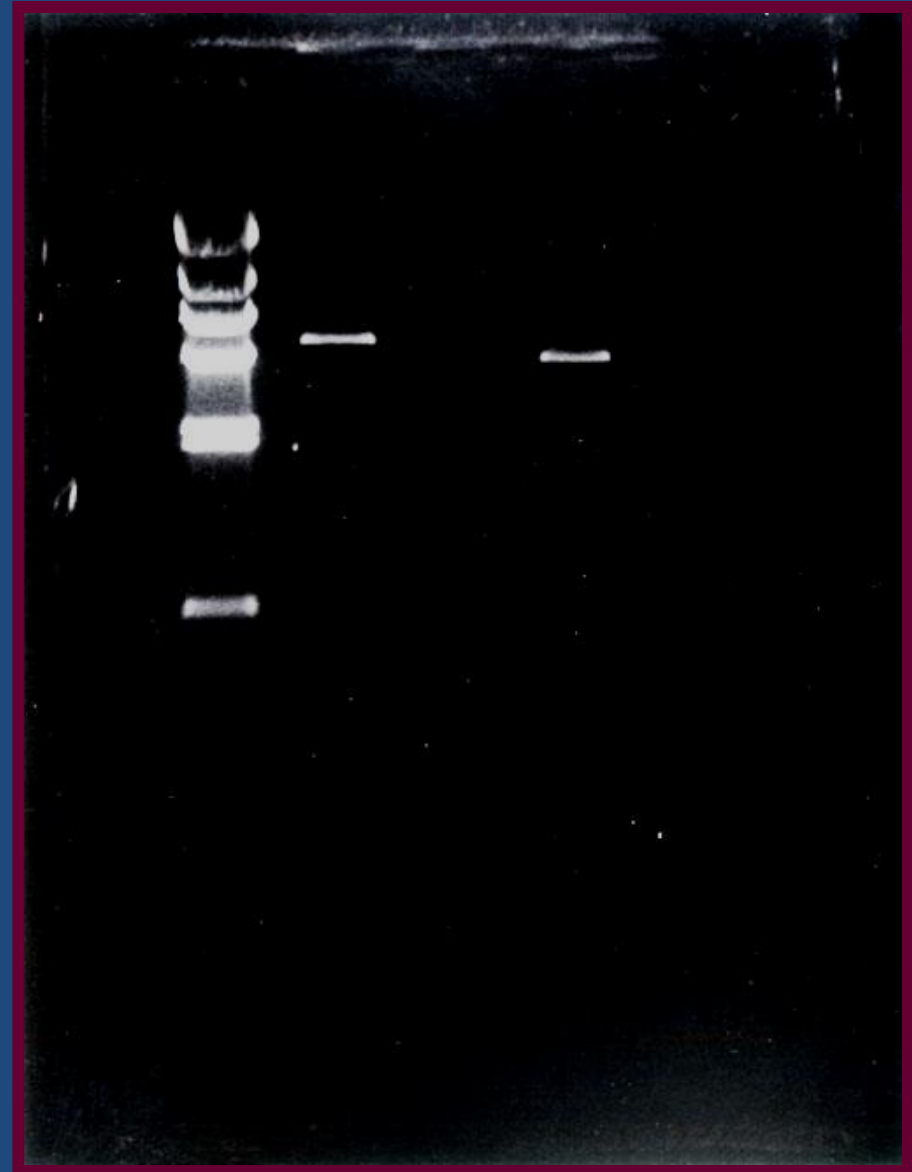
FAX: (650) 225-6000

Depto. Genética UFRGS

Prof<sup>a</sup>. Nance B. Nardi

Prof. Leonardo K. Teixeira

Prof. José Artur Chies



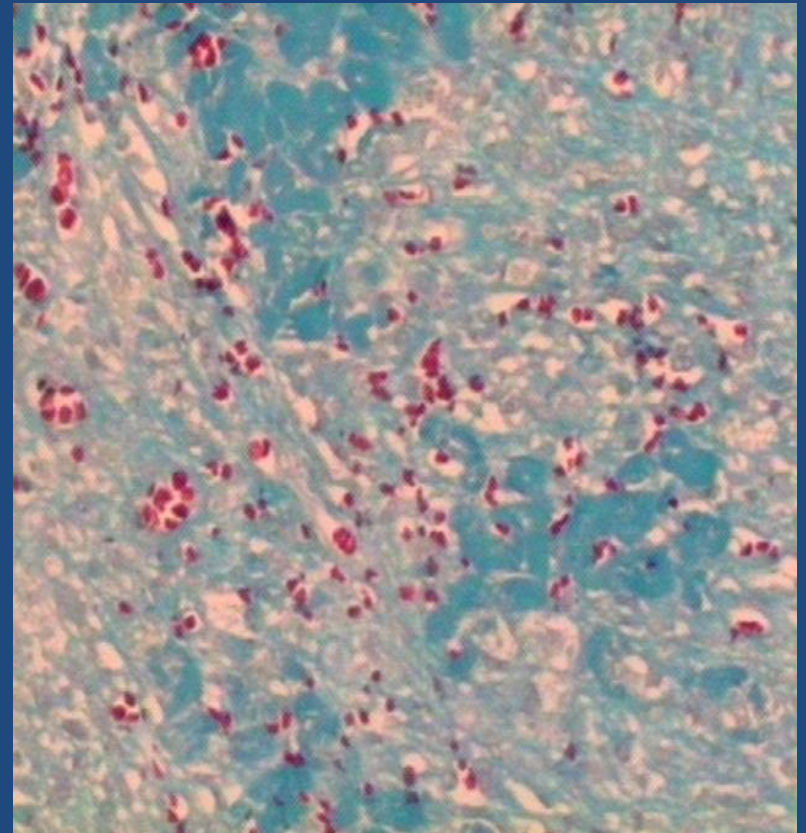
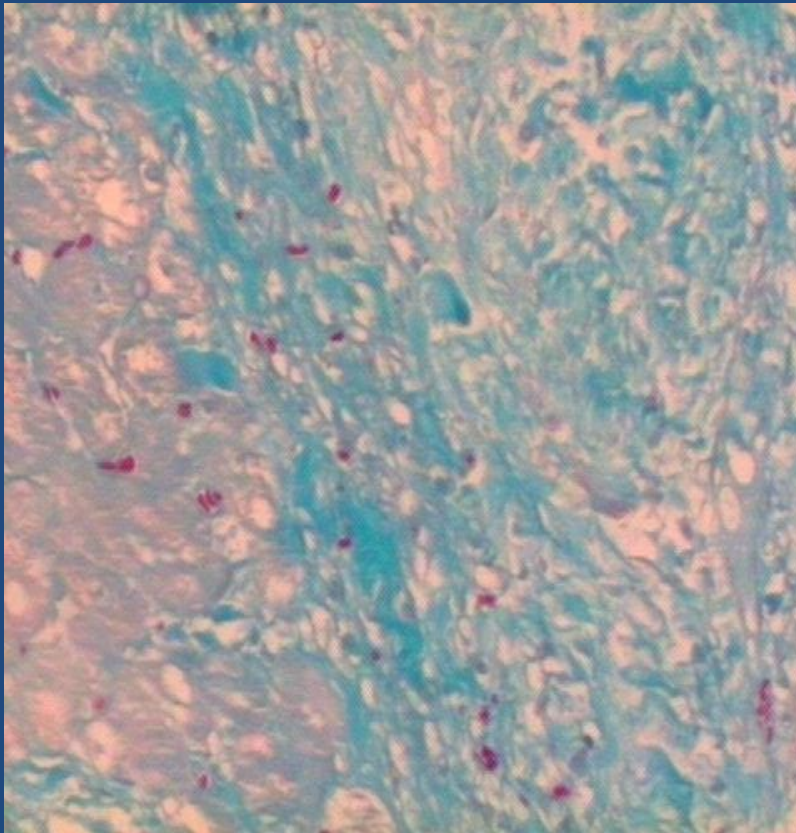
# Histologia

## ÁREA DE TRANSIÇÃO DO IAM

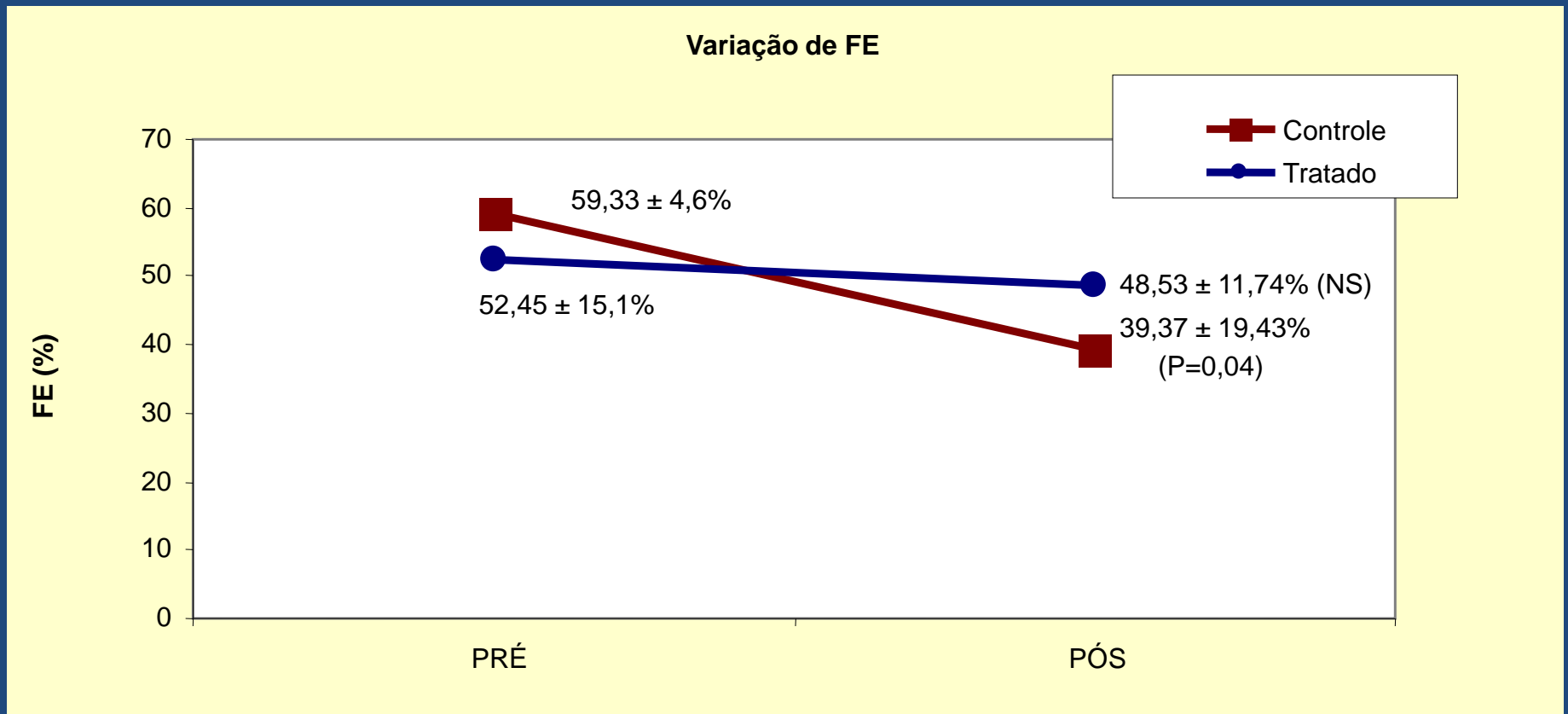
CONTROLE

X

VEGF165



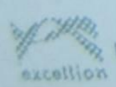
# FE pré e 14 dias após injeção de plasmídeo VEGF165 (grupo tratado) e de solução salina (grupo controle).





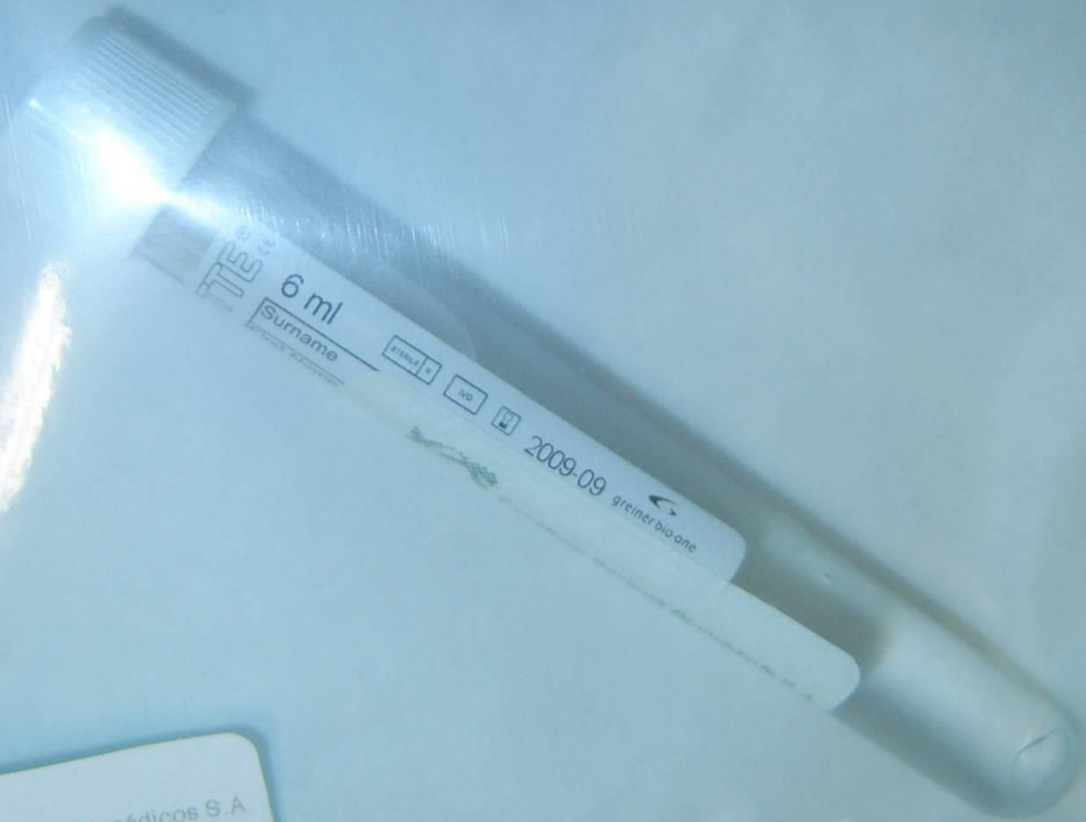
150 mm x 100 m

SISPACK



Excellion Serviços Biosédicos S.A

Amostra: PEX-HV5  
Data do Preparo: 10/02/2009  
Validade: 6 meses  
Armazenamento: -20°C



6 ml

6 ml

Surname

STAMP

NO

2009-09

2009-09

greiner bio one

PREPARAR - EXPOSER TO STEAM  
MAREMMA - COCCOSTO AO MANO  
MAREMMA - ESQUENTO AL VAPOR

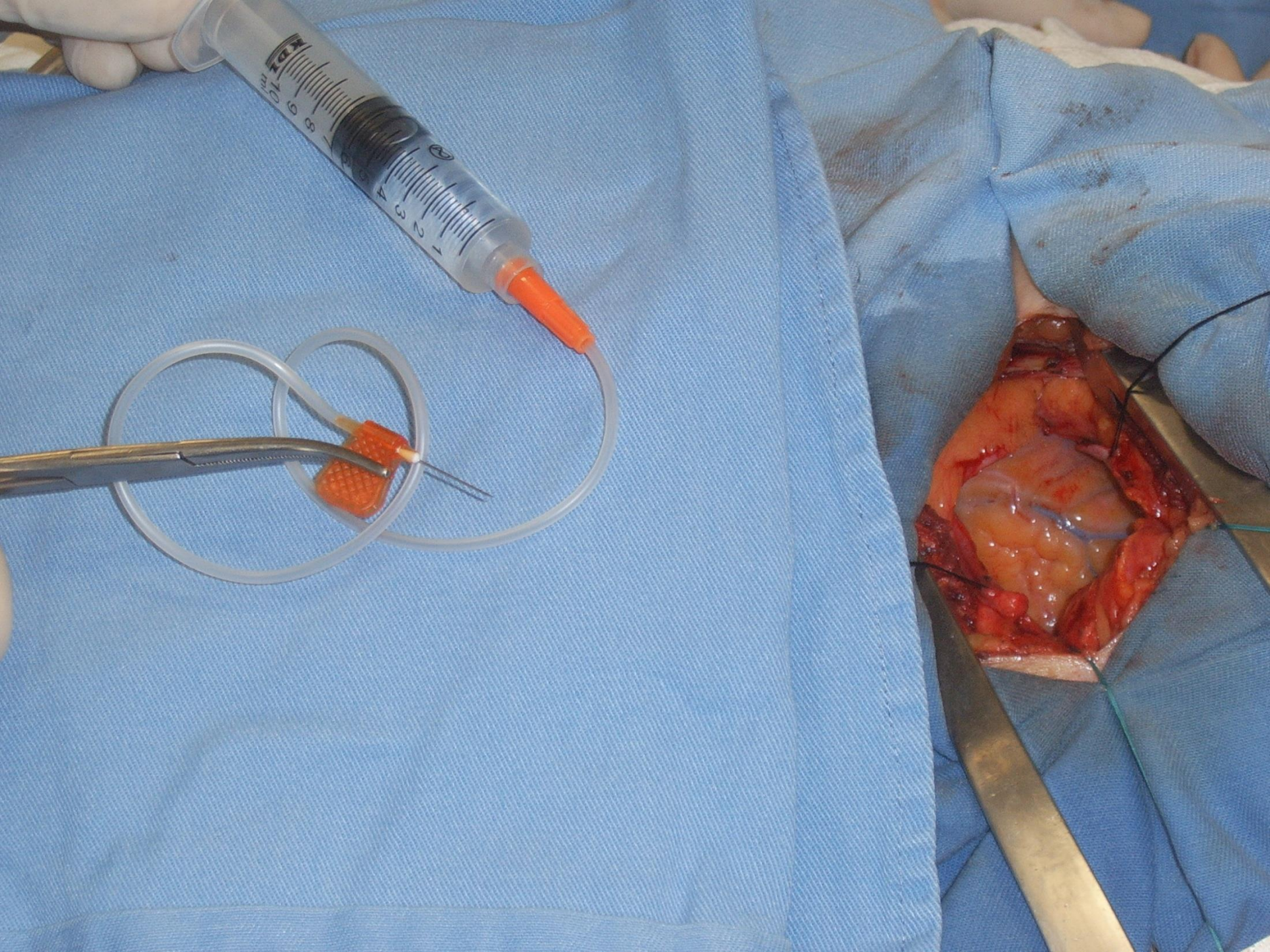
INSTRUCOES DE MANEJO  
- MANEJAR O TUBO EM POSICAO VERTICAL  
- NÃO COLOCAR O TUBO EM CONTACTO COM O REFRIGERADOR

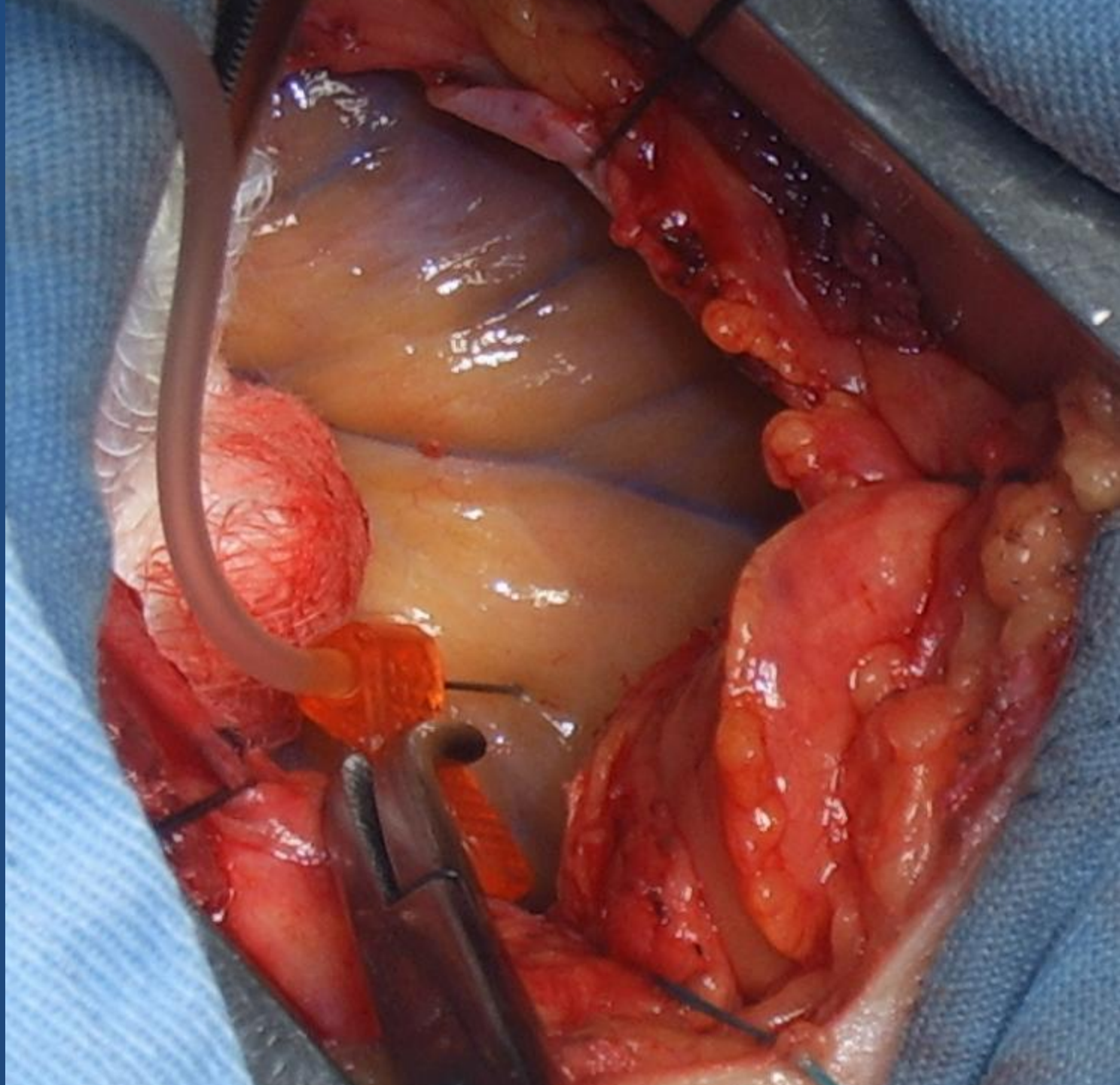
SISPACK

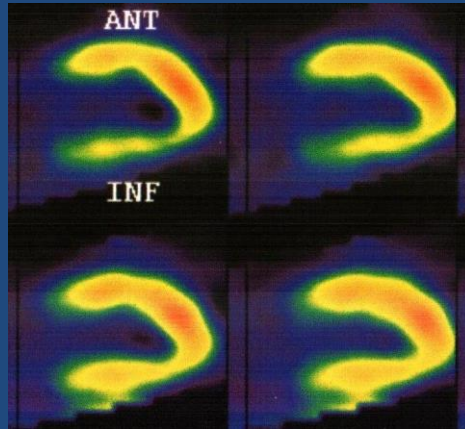
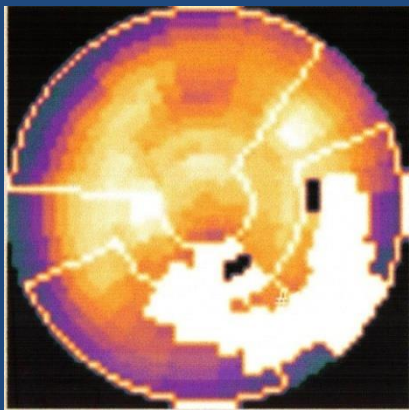
PREPARAR - EXPOSER TO STEAM  
MAREMMA - COCCOSTO AO MANO  
MAREMMA - ESQUENTO AL VAPOR

STI





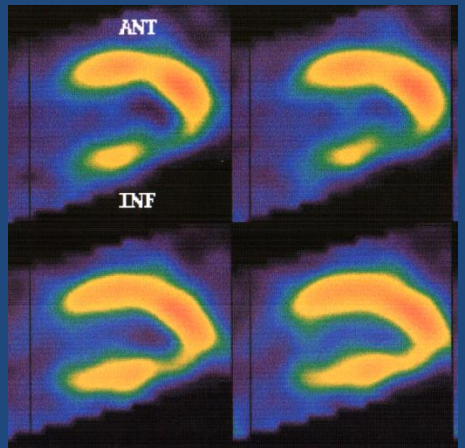
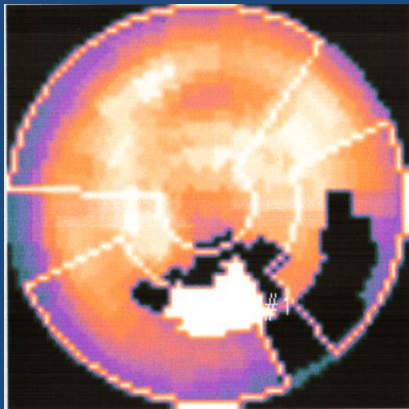




## Pré

NYHA IV / CCSA IV / QQQV 61

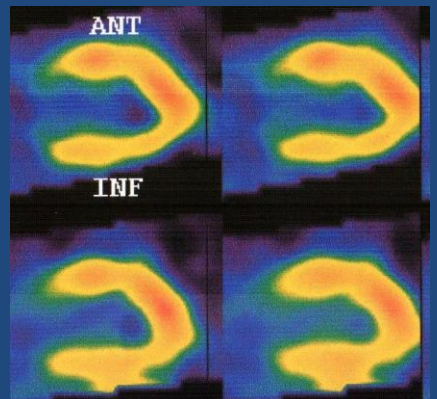
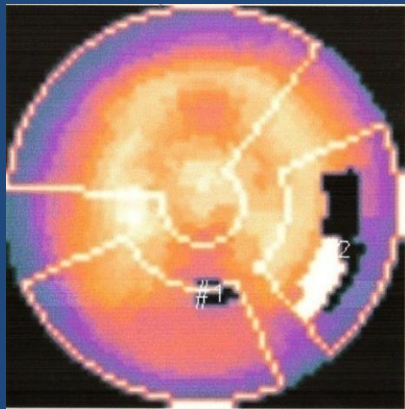
Etapas = 0 ; 2,7 METS



## 1Mês PO

NYHA II / CCSA II / QQQV 36

Etapas = 2 ; 6,7 METS

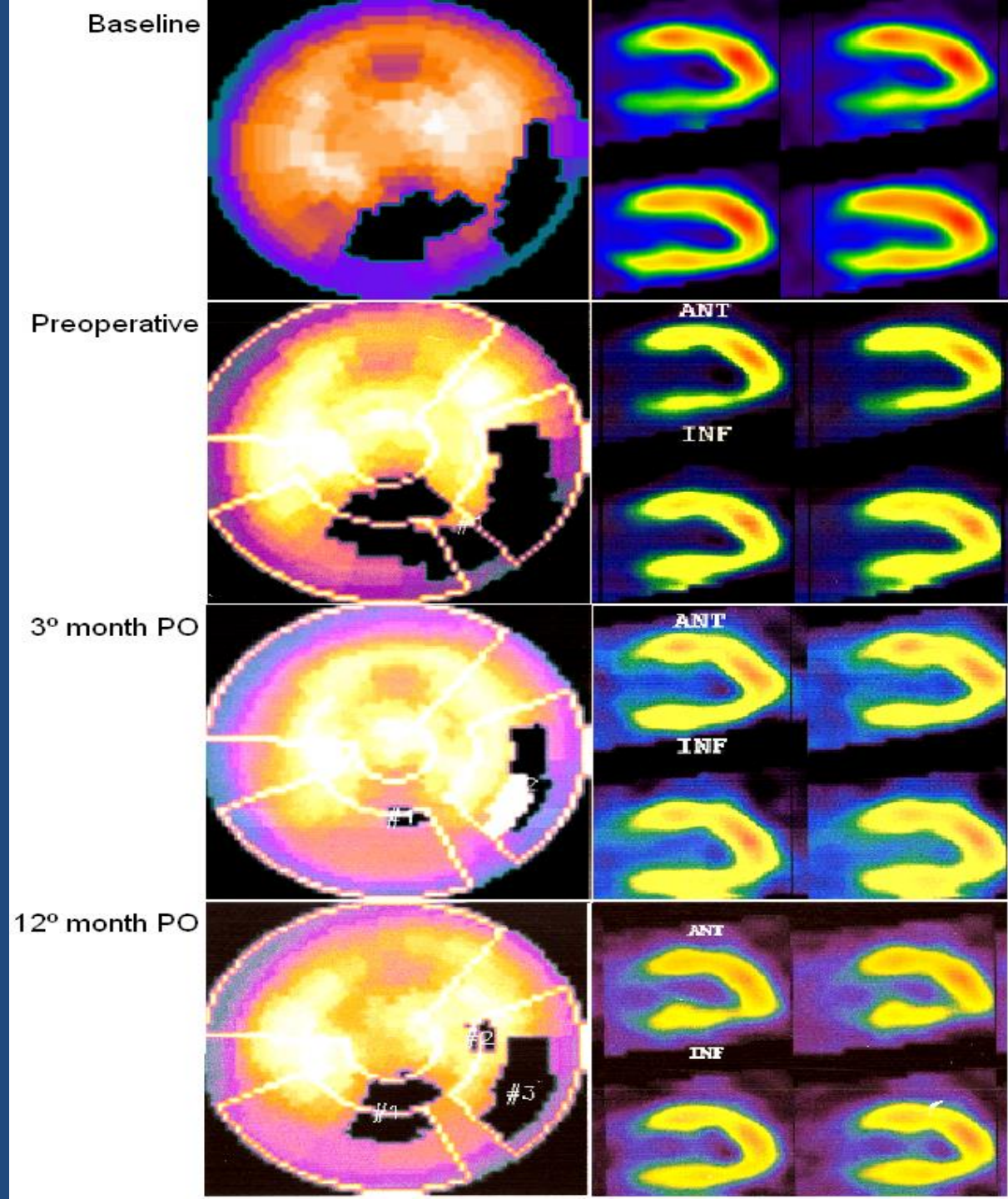


## 3º Mês PO

NYHA II / CCSA II / QQQV 29

Etapas = 2 ; 6,7 METS

**Figure 3:**  
SPECT scan  
Myocardial  
Perfusion



- **Tratamento seguro e viável**
- **Significativa melhora dos sintomas**
- **Tendência de melhora em teste ergométrico e em tolerância ao exercício**
- **Tendência de alteração de perfusão a médio prazo nesta avaliação preliminar**



# Fundação Universitária de Cardiologia Instituto de Cardiologia do Rio Grande do Sul

