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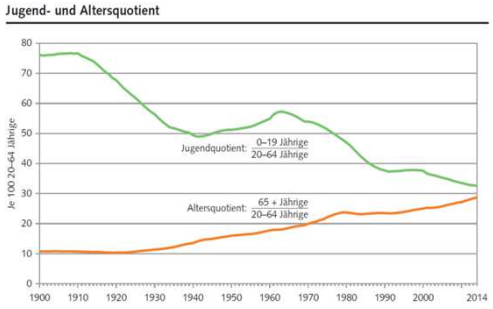
Kardiologie

Ärzte-Fortbildung Arlesheim 25.8.2016

# Interventionelle Therapie der schweren Mitralinsuffizienz

Raban Jeger, Kardiologie USB

## Wir werden immer älter….!
Demographische Entwicklung Schweiz

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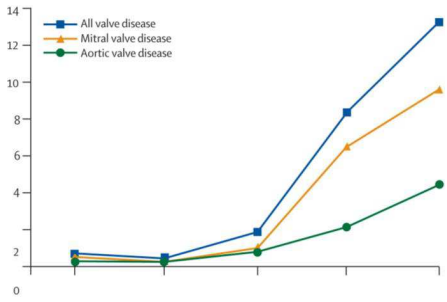
Swiss Federal Bureau of Statistics

## …aber unsere Klappen auch!
Epidemiologie valvuläre Herzkrankheit

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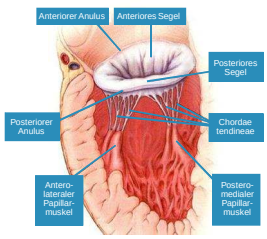
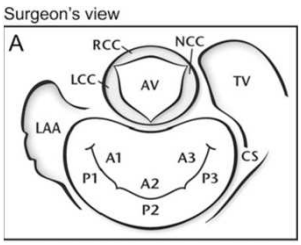
Nkomo VT, et al. *Lancet*. 2006;368:1005-11.

## Mitralklappe
Anatomie




**Mitralklappenapparat:**
Anulus, Segel, Chordae tendineae, Papillarmuskel




**Asymmetrische Klappe:**
Anteriores Segel mit grösserer Oberfläche aber kleinerem Anteil an der Zirkumferenz

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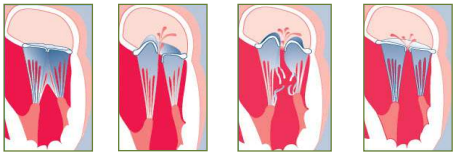
## Mitralinsuffizienz
Einteilung

- **Primäre oder strukturelle Mitralinsuffizienz:** Anatomischer Defekt eines Teils des Mitralklappenapparates (Anulus, Segel, Chordae oder Papillarmuskel)
- **Sekundäre oder funktionelle Mitralinsuffizienz:** Linksventrikuläre Dysfunktion und Dilatation



Prolaps

Sehnenfadenabriss (flail leaflet)

**Normale Mitralklappe**

**Strukturelle Mitralinsuffizienz**

**Funktionelle Mitralinsuffizienz**

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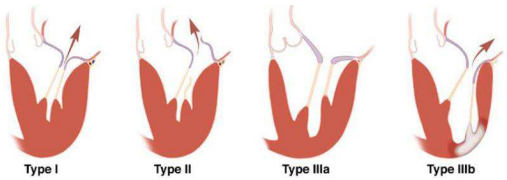
## Mitralinsuffizienz
Carpentier-Klassifikation




| | |
|---|---|
| Type I | Normal leaflet motion |
| Type II | Excess leaflet motion (leaflet prolapse) |
| Type III | Restricted leaflet motion |
| IIIa | Restricted opening |
| IIIb | Restricted closure |

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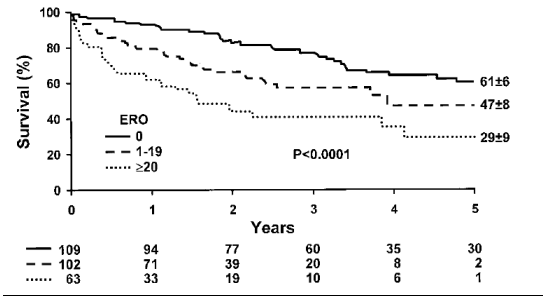
## Funktionelle Mitralinsuffizienz nach Infarkt
Regurgitationsvolumen und Prognose

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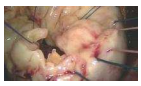
Grigioni, F. et al. *Circulation*. 2001;103:1759-1764.

## Schwere Mitralinsuffizienz
Therapieoptionen

**Konservativ**
- Reduktion Afterload (ACE-Hemmer)
- Ev. Resynchronisation bei Dyssynchronie

**Chirurgisch**
- Mitralklappenrekonstruktion
- Mitralklappenersatz



| | Aortic stenosis *n*=512 | Aortic regurgitation *n*=119 | Mitral stenosis *n*=112 | Mitral regurgitation *n*=155 |
|---|---|---|---|---|
| Mechanical prosthesis (%) | 49.0 | 76.5 | 58.0 | 43.2 |
| Bioprosthesis (%) | 50.0 | 17.6 | 4.5 | 10.3 |
| Homograft (%) | 0.6 | 2.5 | 0 | 0 |
| Autograft (%) | 0.4 | 1.7 | 0 | 0 |
| Valve repair (%) | 0 | 1.7 | 3.6 | 46.5 |
| Percutaneous intervention (%) | 0 | 0 | 33.9 | 0 |
| Associated procedures | | | | |
| – CABG (%) | 33.0 | 15.1 | 7.1 | 31.6 |
| – Total aorta replacement (%) | 0.6 | 19.3 | 0 | 0 |
| – Anti-arrhythmic surgery (%) | 0.2 | 0.8 | 4.5 | 1.9 |

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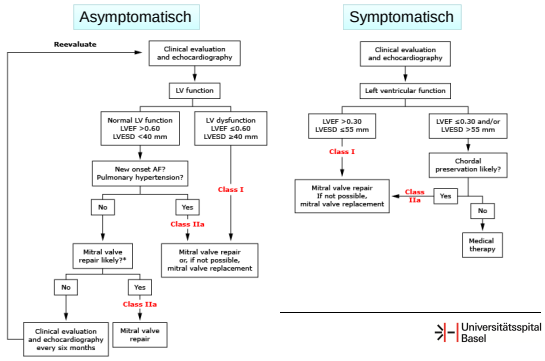
Bonow, RO et al. *Circulation*. 2008;118;e523-e661.
Iung B et al. Eur Heart J. 2003;24:1231-1243.

## Schwere Mitralinsuffizienz
Indikation zu Mitralklappenrekonstruktion/-ersatz

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## Schwere Mitralinsuffizienz
Mitralklappenrekonstruktion/-ersatz

- **Operationsindikationen**
  - *Symptomatische* Patienten wenn LVEF ≥30% oder LVESD ≤55 mm (Class I)
  - *Asymptomatische* Patienten wenn LVEF ≤60% oder LVESD ≥40 mm (Class I) bzw. bei neu aufgetretenem Vorhofflimmern oder pulmonal-arterieller Hypertonie (PAPs >50 mmHg; Class IIa)
- **Perioperative Mortalität**
  - Tiefe perioperative Mortalität (2-3%) und gute Langzeitergebnisse bei *struktureller Mitralinsuffizienz*
  - Erhöhte perioperative Mortalität (6-10%) und fraglicher Benefit bei *funktioneller Mitralinsuffizienz*

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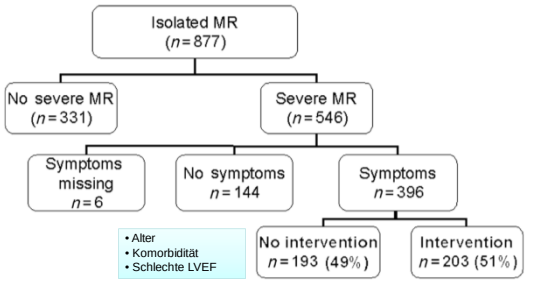
Enriquez-Sarano M et al. *Circulation*. 1995;91:1022-1028; GJ Cooper et al. *Br Heart J*. 1991;66:156-160; Enriquez-Sarano M et al. *Circulation*. 1995;91:1022-1028; Cohn LH et al. *J Thorac Cardiovasc Surg*. 1994;107:143-150; Gillinov AM et al. *J Thorac Cardiovasc Surg*. 2001; 122:1125-1141; Grossi EA et al. *J Thorac Cardiovasc Surg*. 2001; 122:1107-1124.

## Schwere Mitralinsuffizienz
Keine Operation trotz Indikation

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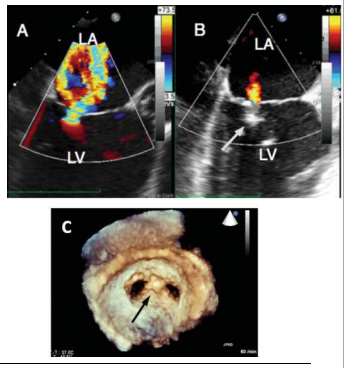
Mirabel M, et al. *Eur Heart J*. 2007;28:1358-1365

## MitraClip
Konzept

- Verbesserung Koaptation der Segel durch Bildung einer interkomissuralen Brücke
- Verringerung Volumenbelastung des linken Ventrikels durch Reduktion Mitralinsuffizienz
- Begrenzung Dilatation Annulus und Ventrikel
- Dauerhaftes Ergebnis

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Franzen O et al, European Heart Journal (2010) 31, 1373–1381

## MitraClip
## System

- Transcatheter repair of the MV
- Beating heart procedure—no cardiopulmonary bypass
- Allows for real-time positioning and repositioning to optimize MR reduction
- Designed to preserve surgical options
- Femoral venous access
- Limited hospital length of stay compared to that after surgery

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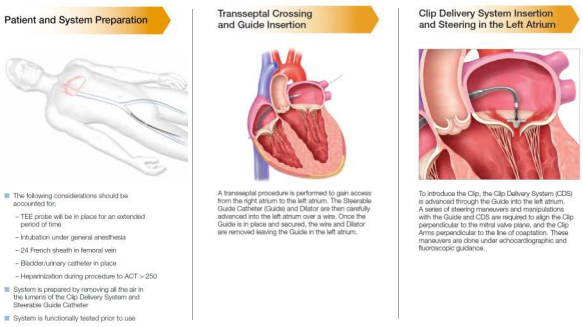
## MitraClip
## Prozedur

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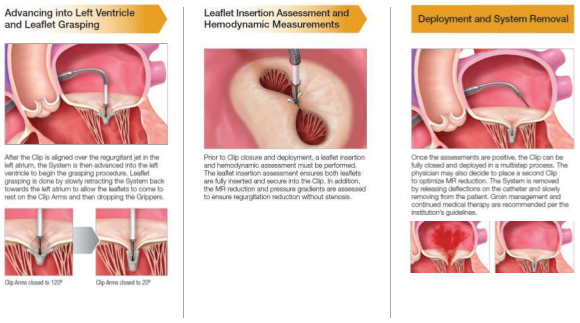
## MitraClip
## Prozedur

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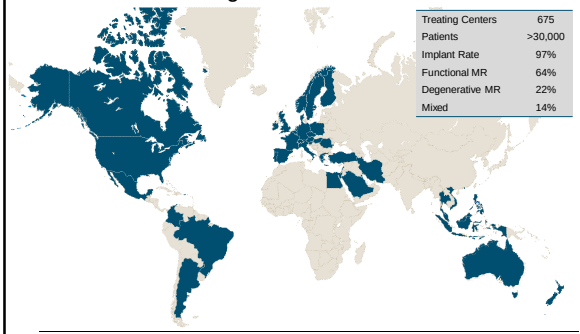
## MitraClip
## Weltweite Erfahrung



| | |
|---|---|
| Treating Centers | 675 |
| Patients | >30,000 |
| Implant Rate | 97% |
| Functional MR | 64% |
| Degenerative MR | 22% |
| Mixed | 14% |

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## EVEREST II Randomized Clinical Trial
### Study Design

279 Patients enrolled at 37 sites

Significant MR (3+-4+)
Specific Anatomical Criteria

↓

Randomized 2:1

**Device Group**
MitraClip System
N=184

**Control Group**
Surgical Repair or Replacement
N=95

**Echocardiography Core Lab and Clinical Follow-Up:**
Baseline, 30 days, 6 months, 1 year, 18 months, and annually through 5 years

NorthShore University HealthSystem Research Institute Evanston Hospital

Investigational device limited by Federal (U.S.) law to investigational use only. PM102827 Rev. A 03/2010

7

## EVEREST II
## Sicherheit

Safety

| Event<br>Major adverse event at 30 days§ | Percutaneous Repair | Surgery | P Value |
|---|---|---|---|
| Any major adverse event | 27 (15) | 45 (48) | <0.001¶ |
| Any major adverse event excluding transfusion | 9 (5) | 9 (10) | 0.23 |
| Death | 2 (1) | 2 (2) | 0.89 |
| Myocardial infarction | 0 | 0 | NA |
| Reoperation for failed surgical repair or replacement | 0 | 1 (1) | 0.74 |
| Urgent or emergency cardiovascular surgery for adverse event | 4 (2) | 4 (4) | 0.57 |
| Major stroke | 2 (1)‖ | 2 (2) | 0.89 |
| Renal failure | 1 (<1) | 0 | 1.00 |
| Deep wound infection | 0 | 0 | NA |
| Mechanical ventilation for >48 hr | 0 | 4 (4) | 0.02 |
| Gastrointestinal complication requiring surgery | 2 (1) | 0 | 0.78 |
| New onset of permanent atrial fibrillation | 2 (1) | 0 | 0.78 |
| Septicemia | 0 | 0 | NA |
| Transfusion of ≥2 units of blood | 24 (13) | 42 (45) | <0.001 |

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Feldman T et al, New England Journal of Medicine 2011; 364(15):1395-406

## EVEREST II
### Wirksamkeit

Efficacy

| Event | Percutaneous Repair | Surgery | P Value |
|---|---|---|---|
| | no. (%) | | |
| **Primary efficacy end point** | | | |
| Freedom from death, from surgery for mitral-valve dysfunction, and from grade 3+ or 4+ mitral regurgitation† | 100 (55) | 65 (73) | 0.007 |
| Death | 11 (6) | 5 (6) | 1.00 |
| Surgery for mitral-valve dysfunction‡ | 37 (20) | 2 (2) | <0.001 |
| Grade 3+ or 4+ mitral regurgitation | 38 (21) | 18 (20) | 1.00 |

Follow-up: 12 Monate

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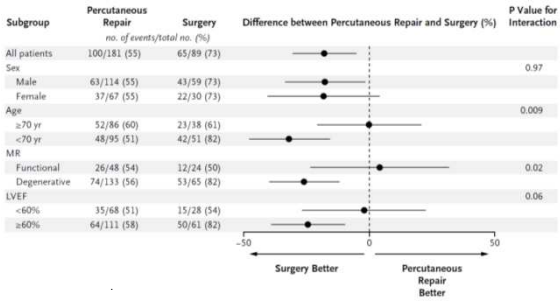
Feldman T et al, New England Journal of Medicine 2011; 364(15):1395-406

## EVEREST II
### Subgroup Analyses for Primary End Point

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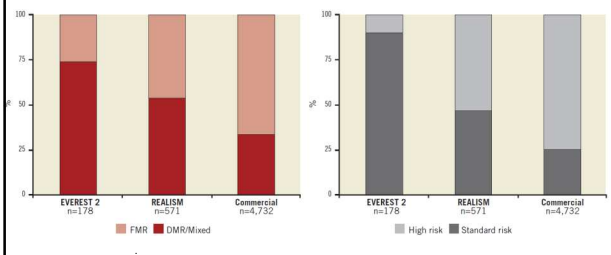
Feldman T et al, New England Journal of Medicine 2011; 364(15):1395-406

## Transcatheter Mitral Valve Interventions
### Patient Selection in Trials and the Real World

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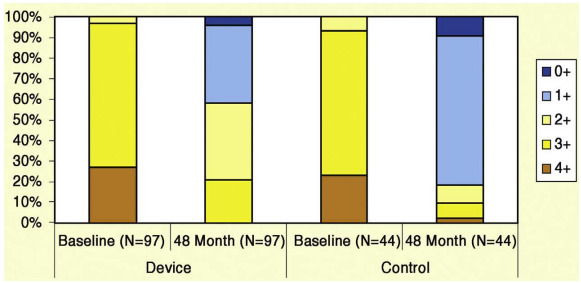
Feldman T et al Ali O, EuroIntervention 2012;8:Q53-Q59

## EVEREST II
### MR Severity at Baseline and 4 Years

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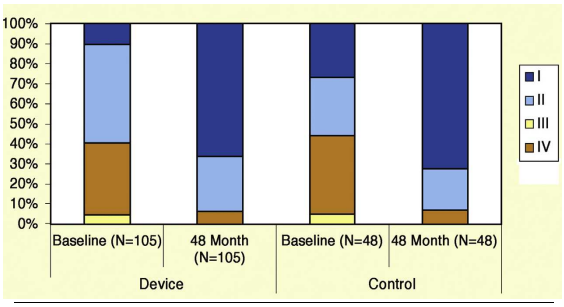
Mauri L et al, J Am Coll Cardiol 2013;62:317–28

## EVEREST II
### NYHA Functional Class at Baseline and 4 Years

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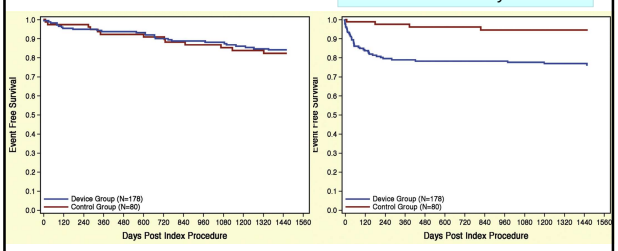
Mauri L et al, J Am Coll Cardiol 2013;62:317–28

## EVEREST II
### Survival 4 Years

Freedom from death

Freedom from surgery to treat mitral valve dysfunction

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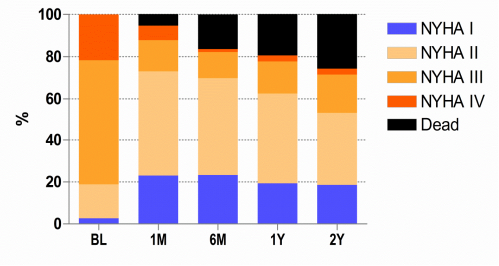
Mauri L et al, J Am Coll Cardiol 2013;62:317–28

## MitraSwiss Registry
Symptoms

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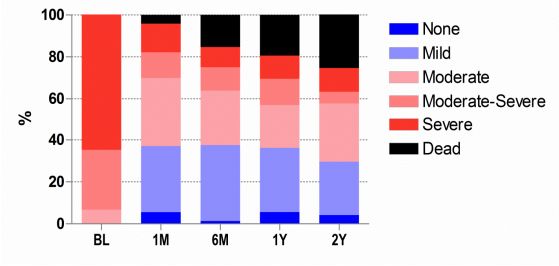
Toggweiler S et al; Open Heart. 2014 Apr 8;1(1):e000056

## MitraSwiss Registry
Mitral Regurgitation Grade

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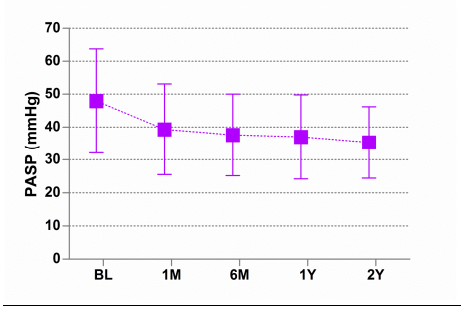
Toggweiler S et al; Open Heart. 2014 Apr 8;1(1):e000056

## MitraSwiss-Registry
Pulmonary Artery Pressure

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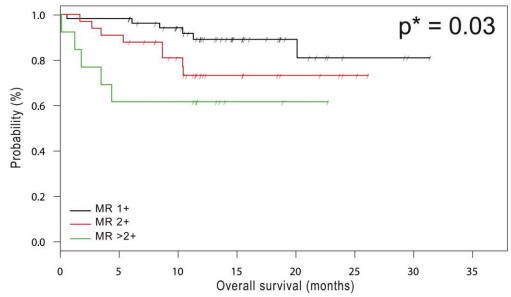
Toggweiler S et al; Open Heart. 2014 Apr 8;1(1):e000056

## MitraSwiss-Registry
Residual MR Grade and Survival

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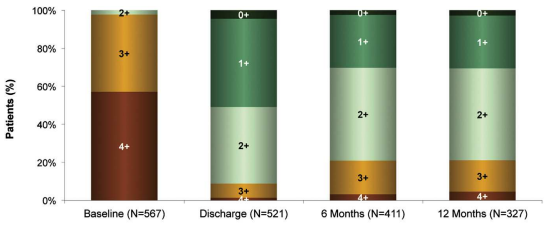
Sürder D et al. Heart 2013;99:1034–1040

## ACCESS-EU Registry
Mitral Regurgitation at Baseline and Follow-Up

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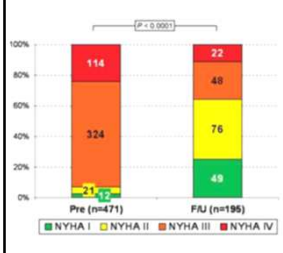
Maisano F et al, J Am Coll Cardiol 2013;62:1052–61

## TRAMI Registry
Symptoms and MACE




Mean Follow-up: 85 Tage

| | n/N (%) |
|---|---|
| Pre-discharge complications | |
| Death | 12/479 (2.5) |
| Stroke | 2/462 (0.4) |
| Repeat percutaneous intervention | 8/463 (1.7) |
| Surgery for failed percutaneous intervention | 16/463 (3.5) |
| Severe bleeding (haemodynamic instability, intracranial, transfusion) | 18/461 (3.9) |
| Transfusion | 48/462 (10.4) |
| Pericardial effusion | 4/461 (0.9) |
| Major vascular complication (requiring surgery or transfusion) | 13/461 (2.8) |
| Minor vascular complication (bleeding, ischaemia) | 20/461 (4.3) |
| Partial clip detachment | 1/461 (0.2) |
| Post-discharge complications | |
| Death | 34/272 (12.5) |
| Surgery for failed percutaneous intervention | 2/111 (1.8) |

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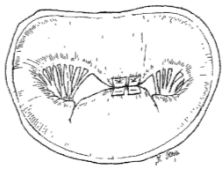
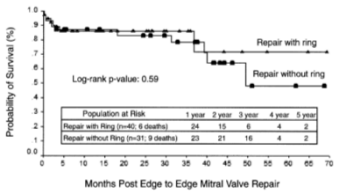
Baldus S et al, European Journal of Heart Failure (2012) 14, 1050–1055

## Surgical Edge-to-Edge Repair
«Alfieri's Stich»

- Surgical connection of anterior and posterior mitral leaflet
- No functional control during surgery
- Repair with vs. without ring



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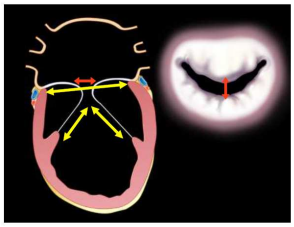
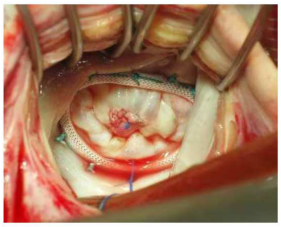
Fucci C et al. Eur J Cardio-thorac Surg 1995: 621-627
Kherani AR et al Ann Thorac Surg 2004;78:73– 6

## Surgical Annuloplasty
Gold Standard for Functional MR Treatment





LV Dilatation:
- Stretching of MV Annulus
- Papillary Muscle Displacement

Annulus Reshaping:
- Implantation of Undersized Ring

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Buellesfeld L, PCR London Valves 2013

## Percutaneous Annuloplasty
Direct and Indirect Techniques

Indirect Annuloplasty

- Cardiac Dimensions Carillon
- Mitral Cerclage Anuloplasty

Direct Annuloplasty

- Valtech Cardioband
- Mitralign
- GDS Accucinch

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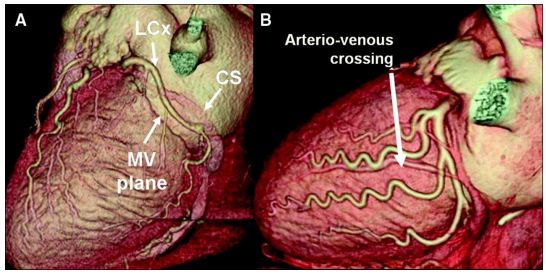
Buellesfeld L, PCR London Valves 2013

## Indirect Annuloplasty
Anatomical Limitations




- Spatial Difference between Coronary Sinus and Mitral Annulus
- Arterio-venous crossing of RCX and Coronary Sinus

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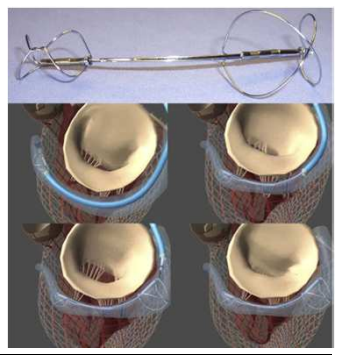
Masson J, Webb J. Circ Cardiovasc Interv 2009;2:140-146

## Indirect Annuloplasty
Carillon

- Jugular venous access
- Self-expandable nitinol distal and proximal
- Anchors connected by a nitinol bridge
- Indirect Annuloplasty via Coronary Sinus
- CE Mark



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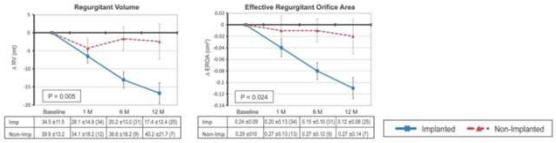
Chiam PTL et Ruiz CE, J Am Coll Cardiol Intv 2011;4:1–13

## Carillon Device
TITAN Trial

| Event | 30 days | | 12 months | |
|---|---|---|---|---|
| | Incidence | Device related | Incidence | Device related |
| Death | 1.9% (1/53) | 0% | 22.6% (12/53) | 0% |
| Implanted | 0% (0/36) | | 22.2% (8/36) | |
| Non-implanted | 6% (1/17) | | 23.5% (4/17) | |
| Myocardial infarction | 0% (0/53) | | 4% (2/53) | 0% |
| Cardiac perforation | 0% (0/53) | 0% | 0% (0/53) | 0% |
| Device embolization | 0% (0/53) | 0% | 0% (0/53) | 0% |
| Surgery due to device | 0% (0/53) | 0% | 0% (0/53) | 0% |
| Overall MAE rate | 1.9% (1/53) | 0% | 26.4% (14/53) | 0% |

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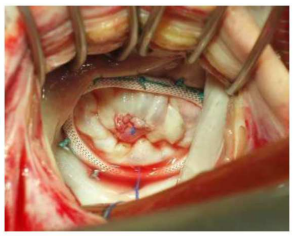
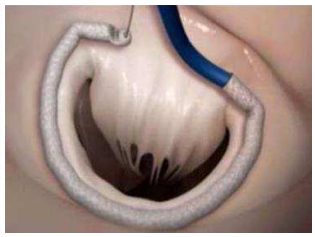
Siminiak T et al, European Journal of Heart Failure (2012) 14, 931–938

## Direct Annuloplasty
### Theoretical Advantages

- Direct approach to the annulus with more accurate prediction of treatment effect
- Closest copy to the surgical gold standard

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Buellesfeld L, PCR London Valves 2013

## Direct Annuloplasty
### Different Techniques

Focal | Semi-circular | Fully Circular

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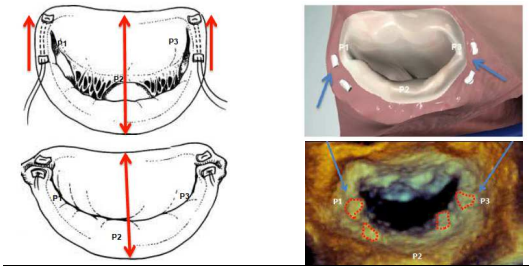
Buellesfeld L, PCR London Valves 2013

## Focal Direct Annuloplasty
### Mitralign

Kay-Wooler Annuloplasty | Plicated Pledget Pair

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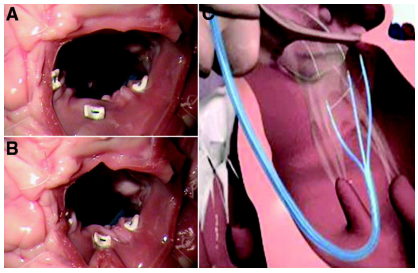
## Focal Direct Annuloplasty
### Mitralign




- Two pairs of surgical pledgets delivered retrogradely to the posterior mitral annulus
- Feasibility and CE-Mark study ongoing

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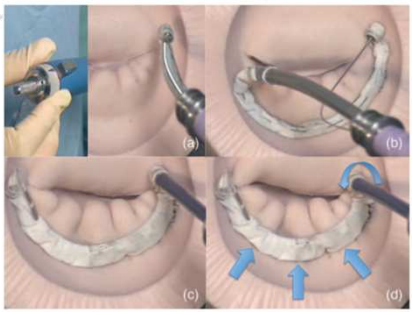
Masson J, Webb J. Circ Cardiovasc Interv 2009;2:140-146

## Semi-Circular Direct Annuloplasty
### Valtech Cardioband

- Venous access
- Transseptal or direct transatrial approach
- Flexible catheter
- Supra-annular fixation
- Individual adjustment
- CE Mark

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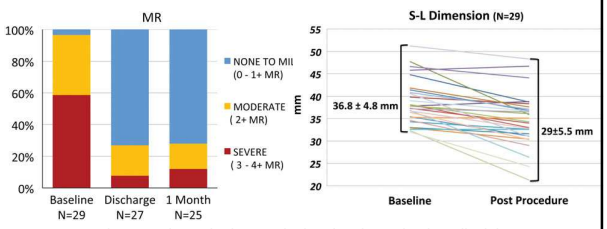
Maisano F et al, European Journal of Cardio-Thoracic Surgery 0 (2012) 1–6

## Valtech Cardioband
### First-in-man Pre-CE-mark Feasibility and Safety Trial




- Symptomatic secondary mitral regurgitation despite optimal medical therapy
- Primary efficacy endpoints: technical success rate of implantation, feasibility of the Cardioband adjustment (technical performance), and ability to reduce the annular septolateral dimension and MR grade at hospital discharge and at 30 days

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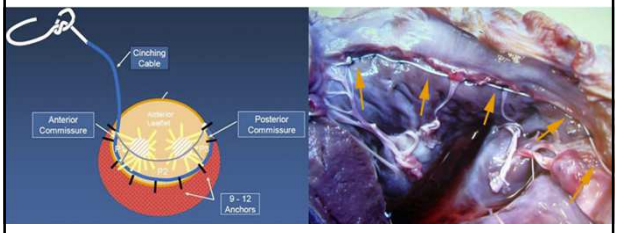
Maisano F et al, European Heart Journal (2016) 37, 817–825

## Semi-Circular Direct Annuloplasty
AccuCinch GDS




- Retrograde approach (aortic)
- Anchors in subannular position, connected with wire
- Adjustmend by tensioning
- Feasibility study ongoing

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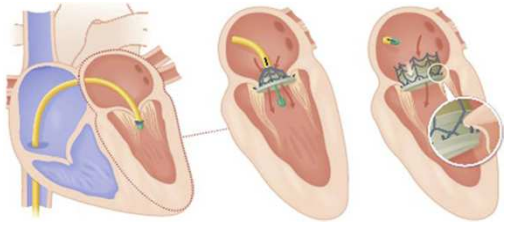
Chiam PTL et Ruiz CE, J Am Coll Cardiol Intv 2011;4:1–13

## Transcatheter Mitral Valve Implantation
CardiAQ Prosthesis



- Delivered transseptally
- AV-loop with an exchange nitinol wire and the use of a customised “steerable snare system” to facilitate the catheter delivery system into the mitral annulus
- Locks onto the inferior and superior surfaces of the mitral annulus

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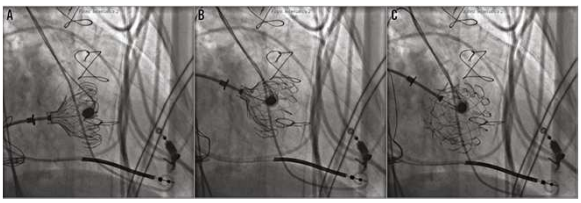
Chiam PTL et Ruiz CE, J Am Coll Cardiol Intv 2011;4:1–13

## Transcatheter Mitral Valve Implantation
CardiAQ Prosthesis




- First procedure description
- 30-day follow-up: NYHA Class I, with good function of the mitral valve bioprosthesis.

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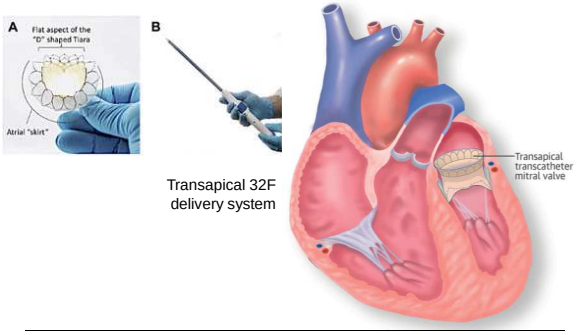
Ussia GP et al., EuroIntervention 2015;11-online publish-ahead-of-print September 2015

## Transcatheter Mitral Valve Implantation
Tiara Prosthesis

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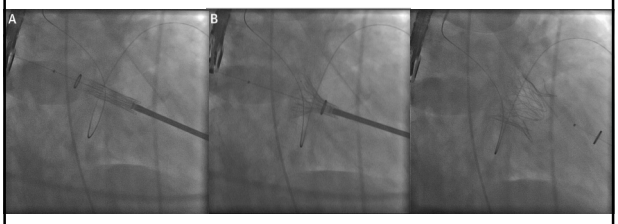
Ole De Backer et al. Circ Cardiovasc Interv. 2014;7:400-409

## Transcatheter Mitral Valve Implantation
Tiara Prosthesis




- First procedure description
- Post-procedural echocardiograms at 48 h, 1 month, and 2 months: excellent prosthetic valve function with a low transvalvular gradient and no left ventricular outflow tract obstruction

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Cheung A et al, J Am Coll Cardiol 2014;64:1814–9

## Interventionelle Therapie schwere Mitralinsuffizienz
Take-home Messages

- Fast 10% der Patienten über 75 Jahre leiden an Mitralinsuffizienz
- Nur 50% aller Patienten mit Mitralinsuffizienz und einer Operationsindikation werden operiert
- Die komplexe Anatomie der Mitralklappe verhindert bisher einfache, effektive technische Lösungen für eine interventionelle Therapie
- MitraClip ist eine etablierte interventionelle Therapieoption bei Hochrisikopatienten mit schwerer Mitralinsuffizienz, v.a. älteren Patienten mit eingeschränkter Pumpfunktion und funktioneller Mitralinsuffizienz
- Eine Anuloplastie der Mitralkappe könnte die klinischen Ergebnisse der interventionellen Therapie weiter verbessern, wobei die direkte Mitralklappenanuloplastie hier gewisse theoretische Vorteile besitzt
- Der interventionelle Mitralklappenersatz ist komplex und bisher technisch noch nicht ganz ausgereift

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