

VALUTAZIONE FUNZIONALE DI VALVOLE CARDIACHE MECCANICHE parte sperimentale

Le malattie delle valvole cardiache si definiscono **valvulopatie** e possono essere di due tipi:

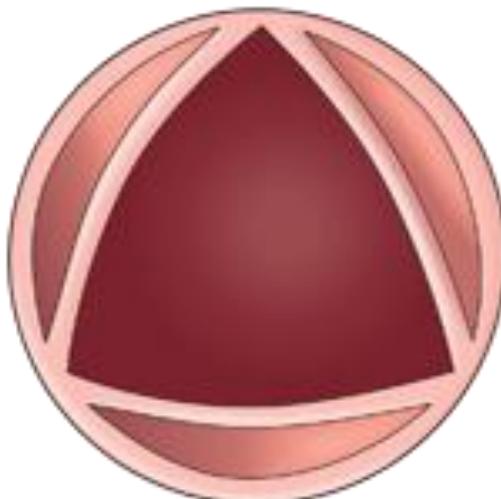
- **stenosi** (incompleta apertura: il sangue passa attraverso un orifizio più piccolo della norma)
- **insufficienza** (incompleta chiusura: parte del sangue torna indietro attraverso la valvola che dovrebbe essere chiusa)

Molto spesso stenosi e insufficienza coesistono, in diversa misura, nella stessa valvola, realizzando la cosiddetta **stenoinsufficienza**

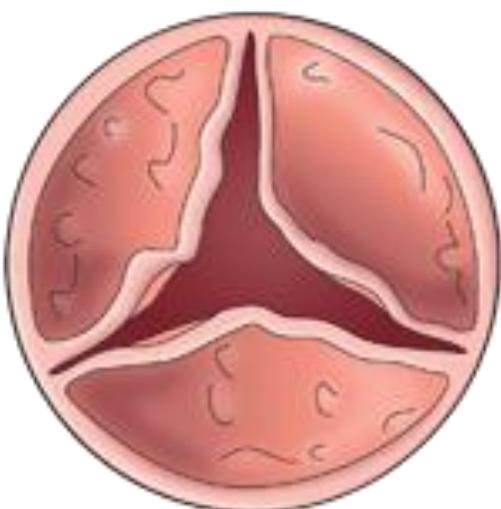
La sostituzione di valvola cardiaca è la più comune procedura chirurgica utilizzata in pazienti che presentano uno stato patologico avanzato

Nel mondo oltre 250.000 pazienti necessitano annualmente di intervento di sostituzione valvolare

**normal
aortic
valve**



**aortic
valve
stenosis**



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open



closed

Si possono distinguere protesi valvolari:

- **meccaniche**: composte principalmente da metallo e carbonio pirolitico
- **biologiche**:
 - ✓ *eterologhe*: composte da tessuto porcino o bovino (valvolare o pericardico)
 - ✓ *omologhe*: valvole umane prelevate da cadavere

Con rare eccezioni le valvole meccaniche sono durevoli, il più delle volte 20-30 anni

Le protesi biologiche solitamente *falliscono* dopo 10-15 anni dall'impianto e devono essere sostituite

Di norma:

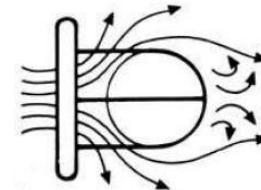
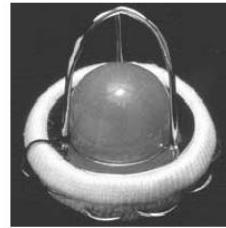
- le protesi valvolari meccaniche sono preferite nei pazienti giovani o con un'aspettativa di vita superiore a 10-15 anni
- le protesi valvolari biologiche sono da preferirsi per pazienti anziani, con un'aspettativa di vita inferiore ai 10-15 anni

Le protesi meccaniche sono **trombogeniche**: il loro utilizzo impone la somministrazione di terapia anticoagulante orale (TAO) a vita

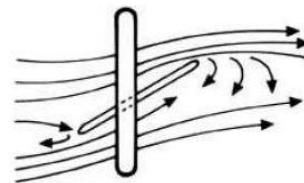
mentre

le protesi biologiche hanno basso/nullo potenziale trombogenico: la terapia anticoagulante non è richiesta

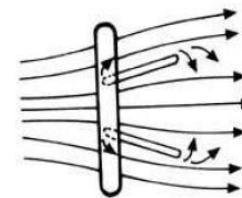
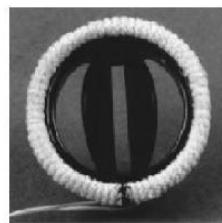
a palla ingabbiata



mono-leaflet



bi-leaflet



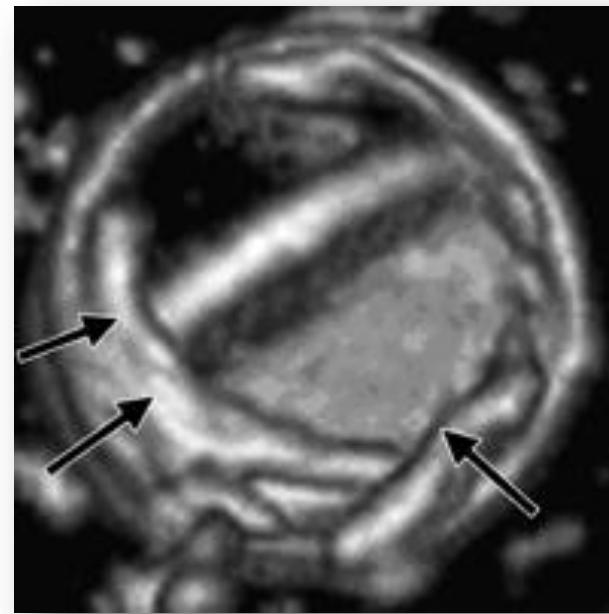
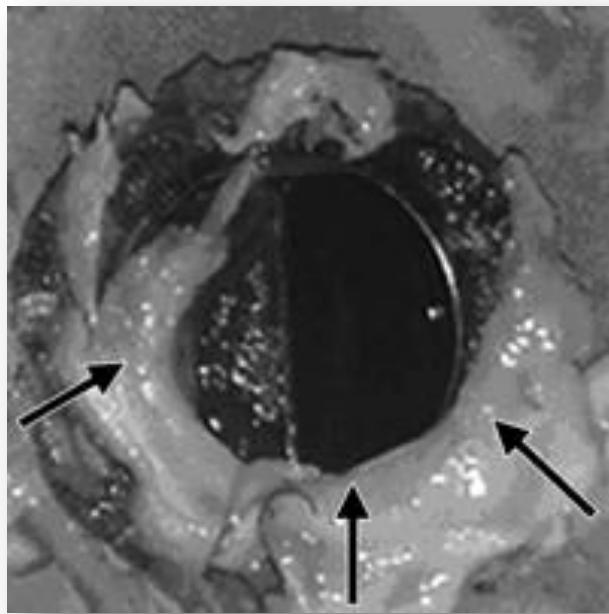
Le più recenti valvole cardiache meccaniche sono dette **bi-leaflet** (due emidischi oscillanti)

I principali elementi costitutivi sono:

- *anello di sostegno* (lega metallica e carbonio pirolitico)
- *anello di sutura* (Dacron)
- due *emidischi (leaflet)* oscillanti incardinati nell'anello



esempi di protesi bileaflet



esempi di **trombosi** valvolare

Prosthetic heart valve thrombosis: key points

- ▶ Prosthetic valve thrombosis (PVT) is a serious complication of valvular replacement associated with significant morbidity and mortality
- ▶ The incidence is higher for mechanical than for biological heart valves (right-sided > left-sided, mitral > aortic). Non-obstructive thrombi are more frequently observed than obstructive thrombi

Valve disease

THROMBOSIS OF PROSTHETIC HEART VALVES: DIAGNOSIS AND THERAPEUTIC CONSIDERATIONS

Raymond Roudaut, Karim Serri, Stephane Lafitte

Heart 2007;93:137–142. doi: 10.1136/hrt.2005.071183

- ▶ The early postoperative period, interruption of anticoagulant therapy for non-cardiac surgery, and pregnancy are particularly high-risk situations for patients with prosthetic heart valves

Valve disease

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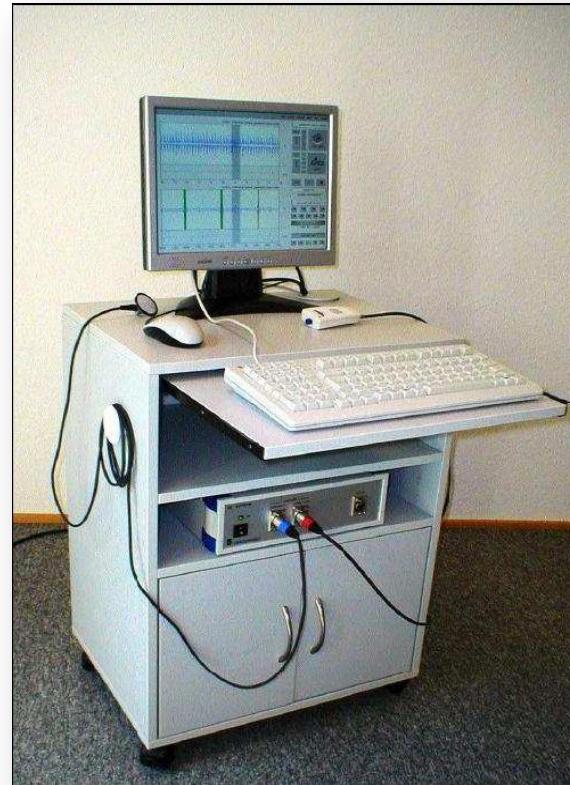
- ▶ Diagnosis is based on cinefluoroscopy (for mechanical valves) and echocardiography. Suggestive findings include reduced or absent leaflet mobility, elevated transprosthetic gradients, decreased effective orifice area and thrombus visualisation
- ▶ Transoesophageal echocardiography (TOE) has an important diagnostic role, particularly in difficult cases, and can differentiate thrombi from pannus formation or strands. TOE is also important in guiding treatment

Valve disease

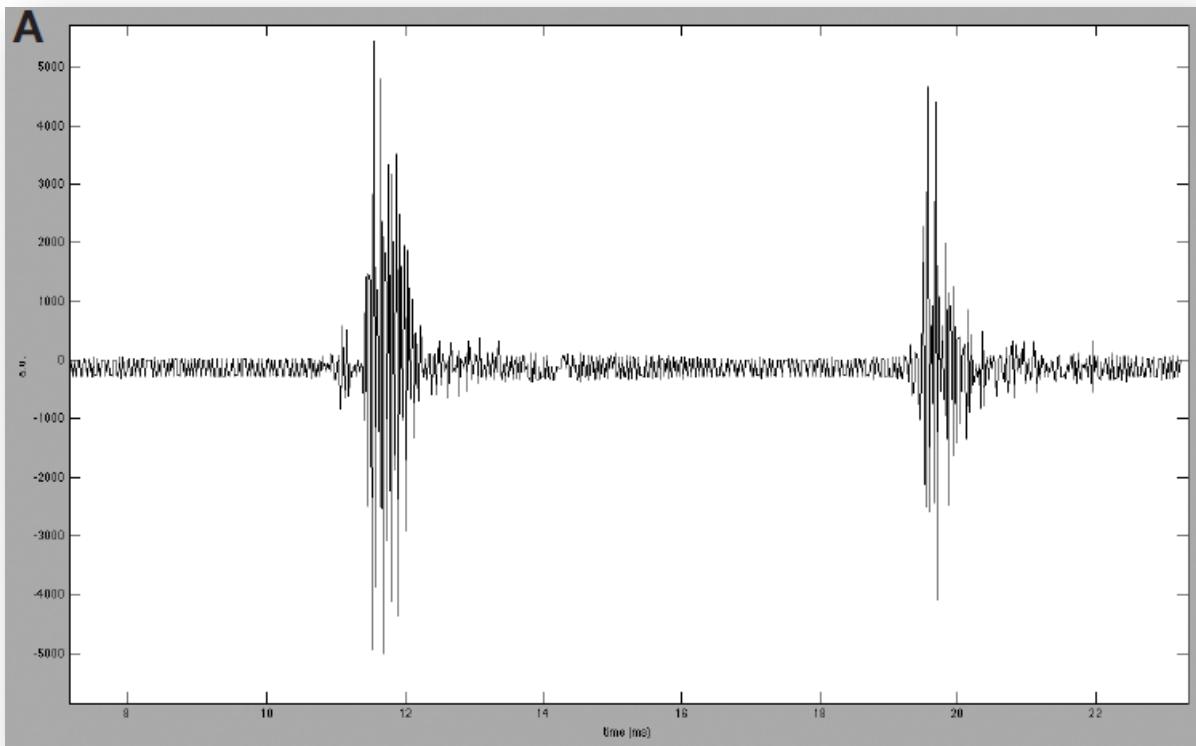
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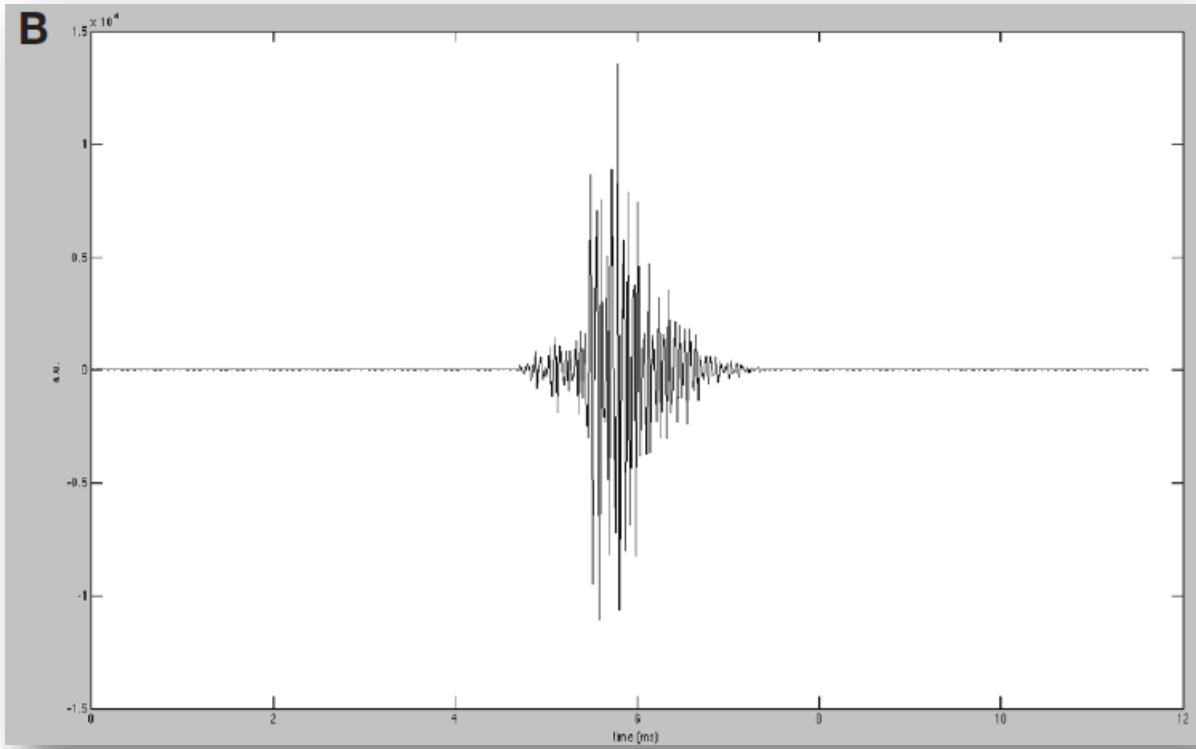
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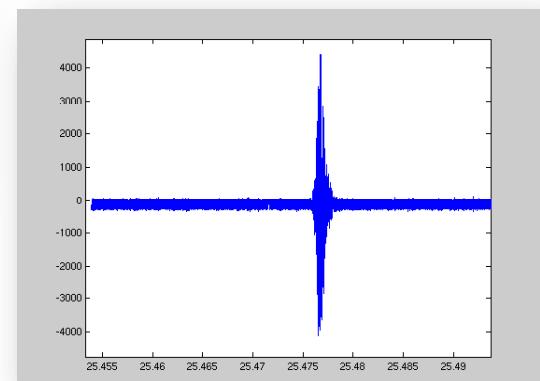
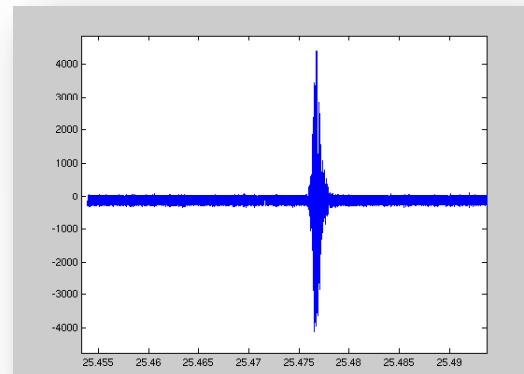
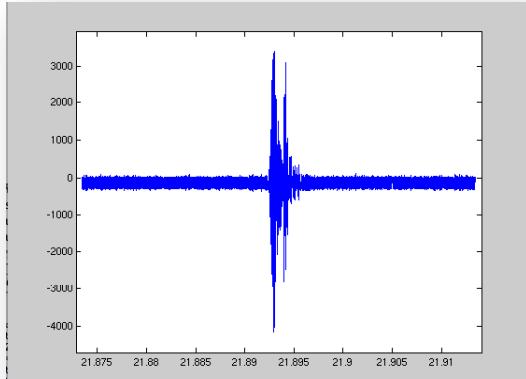
fonocardiografo: Myotis 3C



“suono” di chiusura corretto
di una valvola meccanica biliflet *in vivo*



“suono” di chiusura non corretto
di una valvola meccanica biliflet *in vivo*



“suono” di chiusura classificati
come non corretti o non classificati

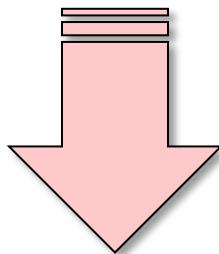
ANALISI MULTIRISOLUZIONE

In accordo con altri lavori presenti in letteratura è stata considerata la **Trasformata Wavelet Continua** (CWT) del segnale operata attraverso la *Wavelet di Morlet*, per garantire una maggiore risoluzione temporale alle basse scale (alte frequenze)

È stato implementato un algoritmo che effettua il pre-processamento del segnale da cui si ottengono i coefficienti della CWT corrispondenti al maggiore contenuto in frequenza del segnale: il riconoscimento e la classificazione dei picchi viene effettuata su questi coefficienti

Myotis	Y	N
Doppio Click	VP = 5	FN = 185
Singolo Click	FP = 0	VN = 30

Sensibilità: 2,6 % ± 2,1%
Specificità: 100% ± 0%
Probabilità assegnazione corretta: 16 % ± 4,8%



CWT	Y	N
Doppio Click	VP = 174	FN = 15
Singolo Click	FP = 12	VN = 19

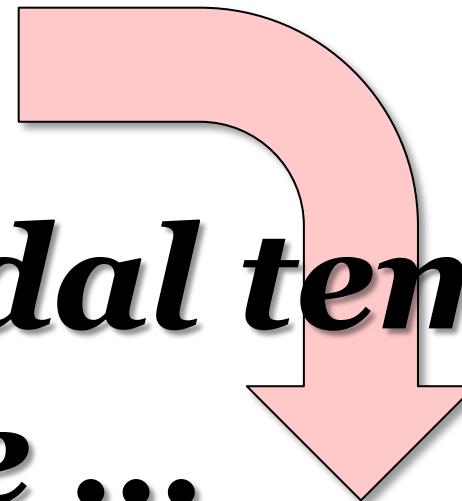
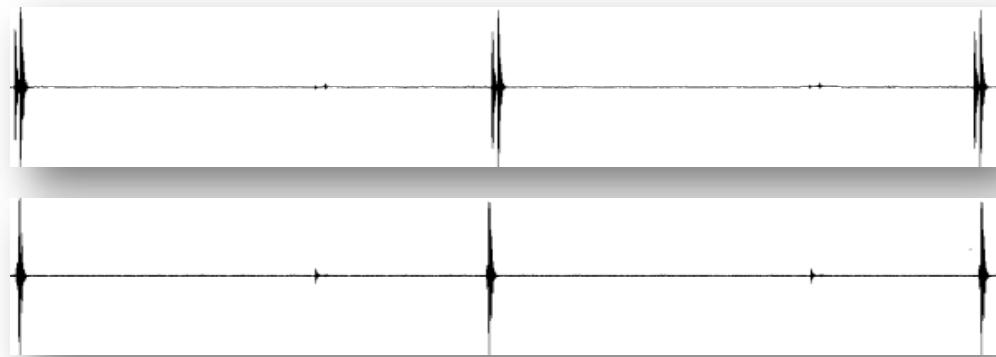
Sensibilità: 92% ± 3,6%
Specificità: 61,3% ± 6,4%
Probabilità assegnazione corretta: 87,8% ± 4,3%

Sensibilità: capacità di identificare correttamente i soggetti malati
Specificità: capacità di identificare correttamente i soggetti sani

Artificial Heart and Cardiac Assist Devices

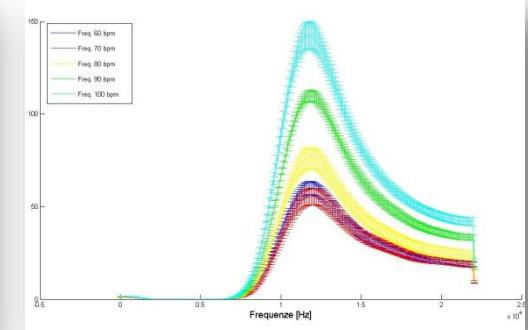
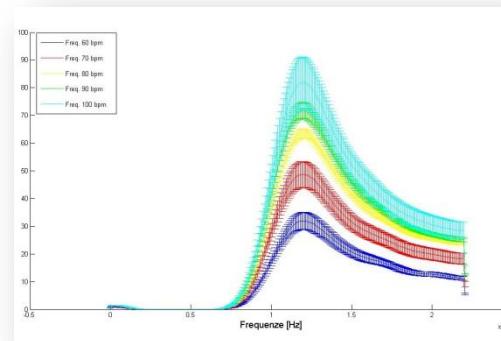
Application of wavelet analysis to the phonocardiographic signal of mechanical heart valve closing sounds

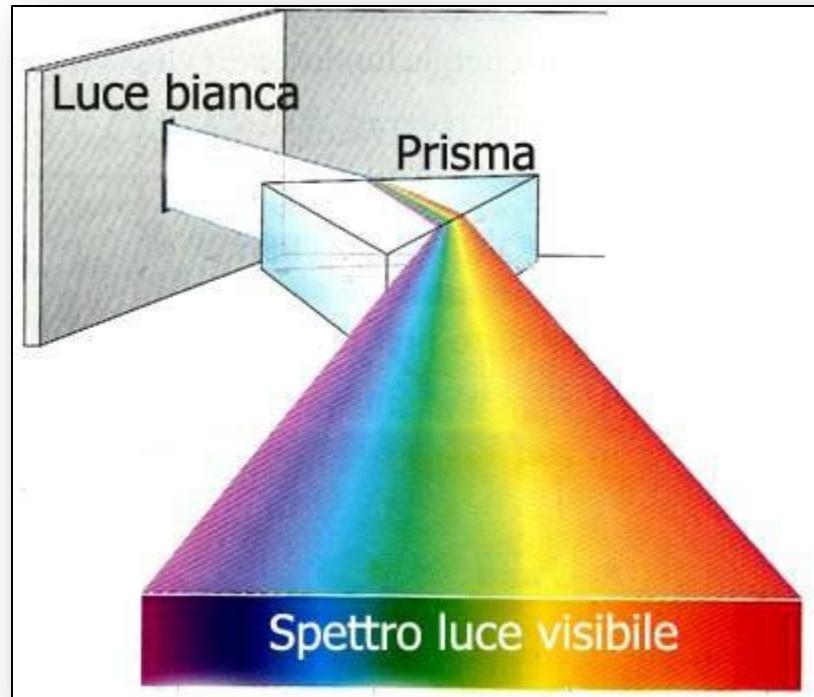
A. BAGNO¹, F. ANZIL¹, V. TARZIA², V. PENG³, A. RUGGERI⁴, G. GEROSA²



... dal tempo

alle frequenze ...

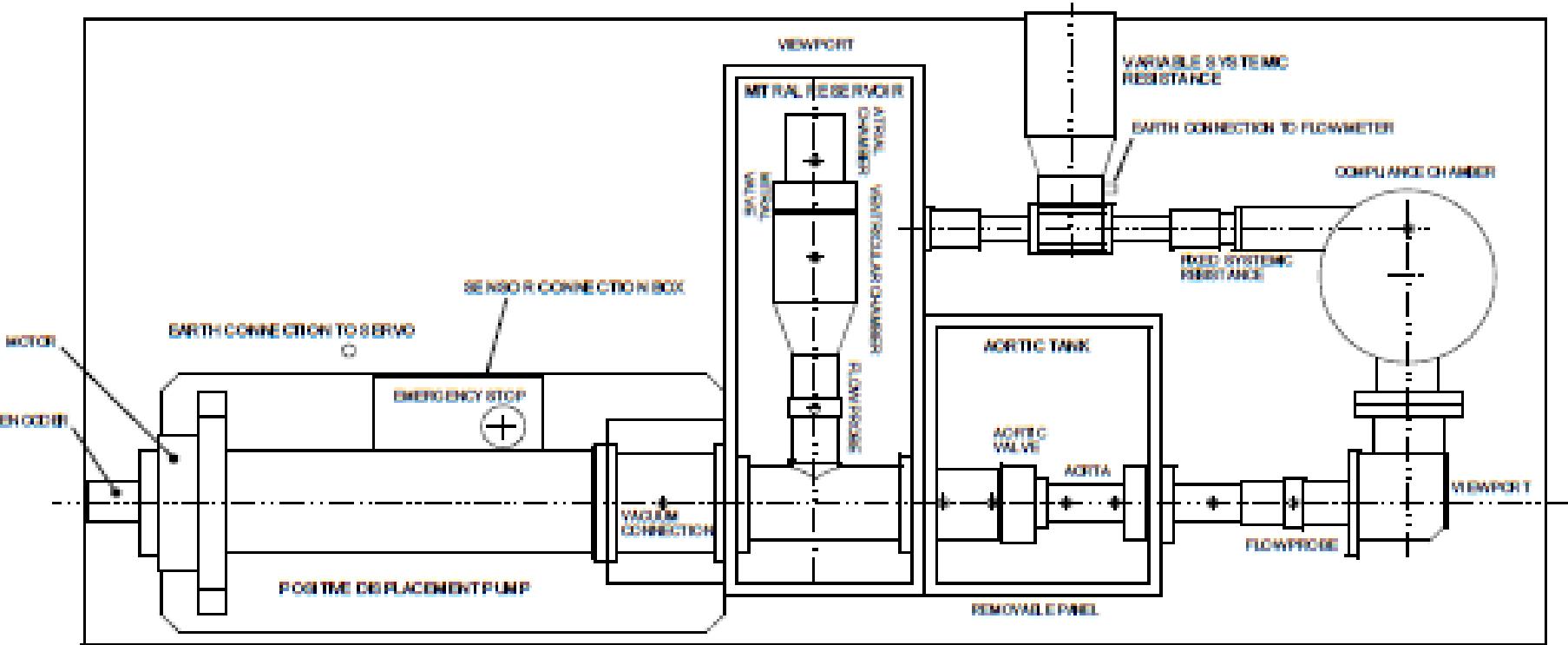




analisi spettrale: l'esempio della luce bianca

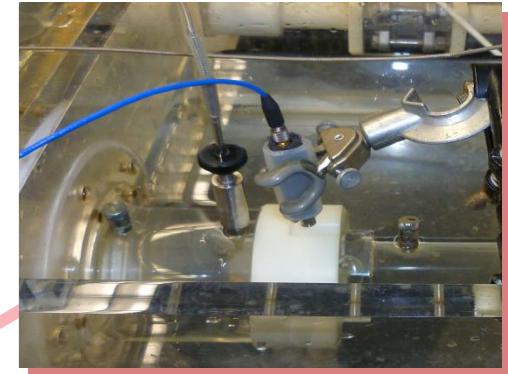
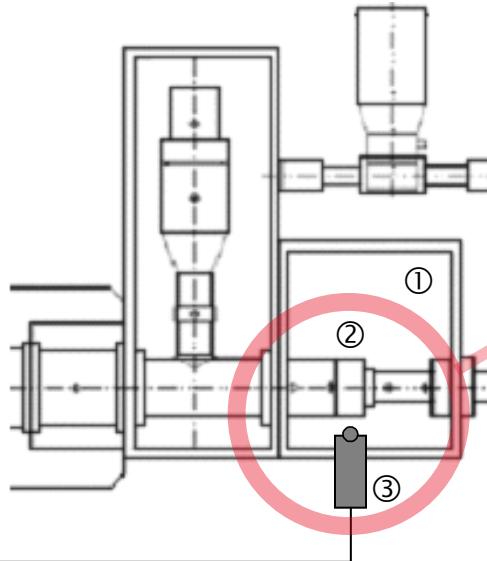
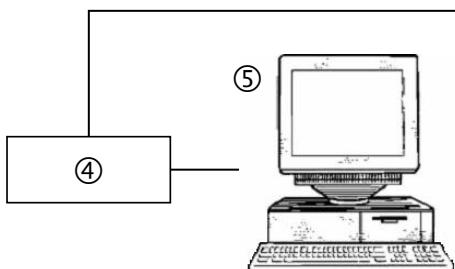
SHEFFIELD PULSE DUPLICATOR

- simula il comportamento del cuore e la circolazione sistemica
- le variazioni volumetriche sono prodotte da una pompa
- si possono impostare frequenza cardiaca e portata



Sheffield pulse duplicator



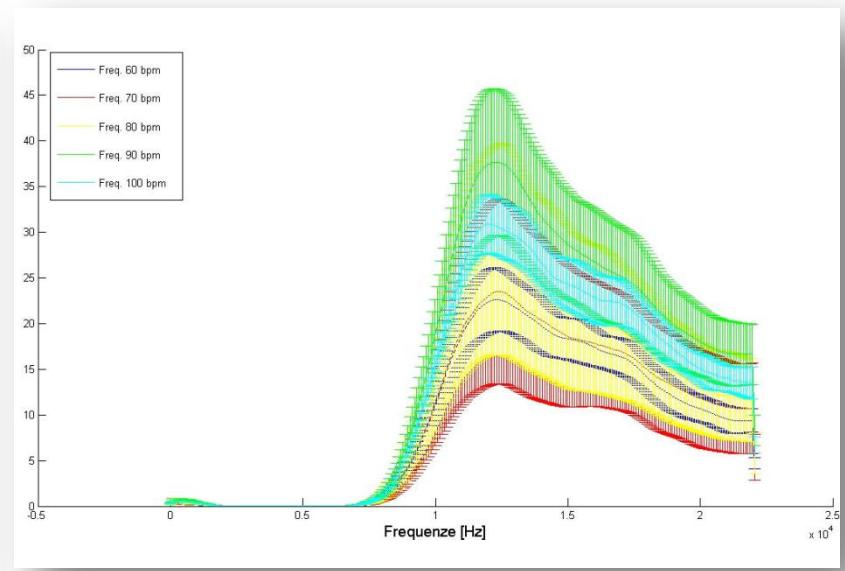
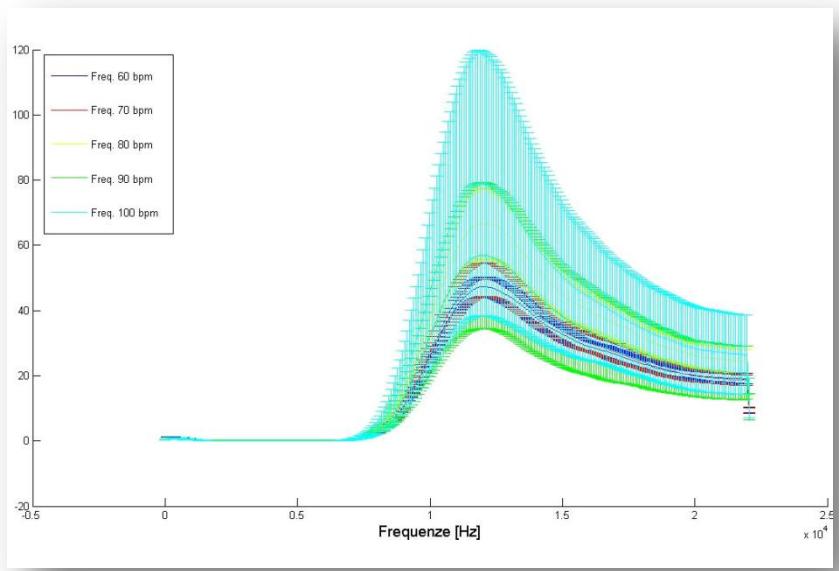


- ① = **camera aortica**
- ② = **valve holder**
- ③ = **trasduttore**
- ④ = **scheda audio**
- ⑤ = **PC**

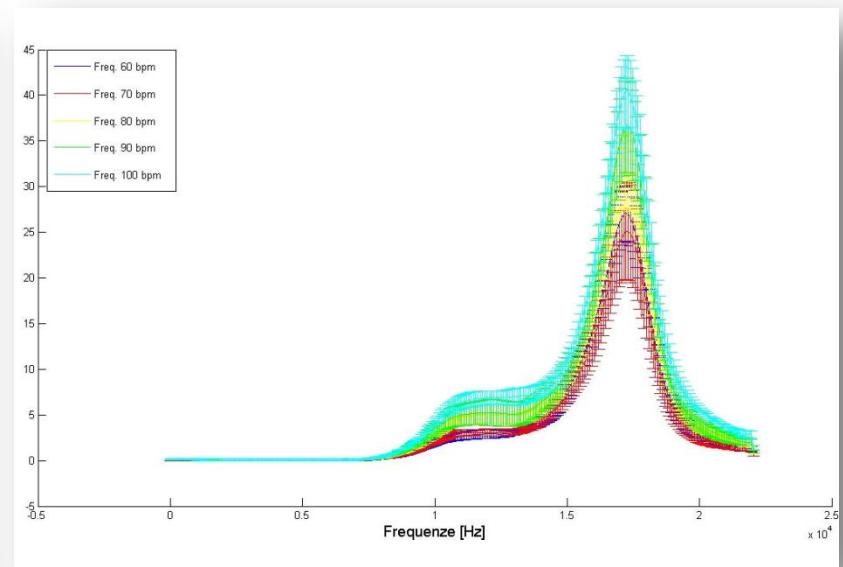
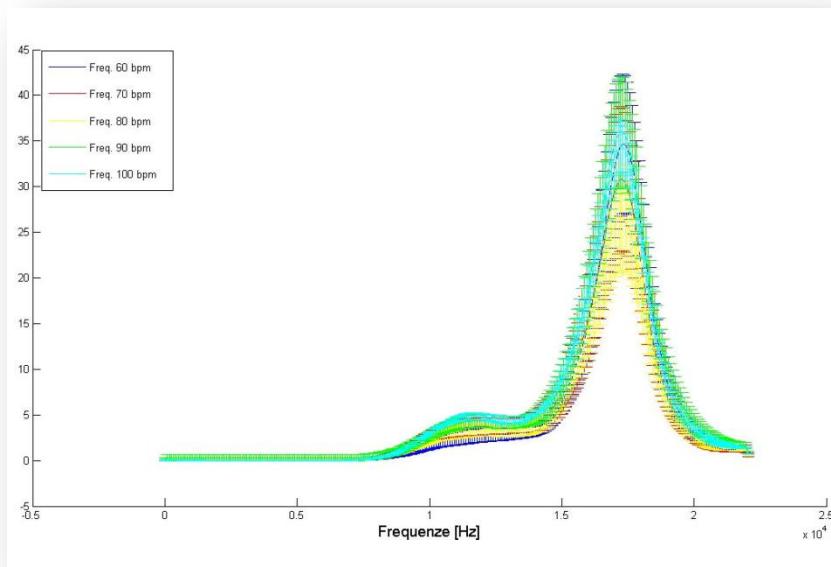
#	gittata (SV) [ml]	battito [bpm]	portata [l/min]
1		60	3.0
2		70	3.5
3	50	80	4.0
4		90	4.5
5		100	5.0
6		60	3.6
7		70	4.2
8	60	80	4.8
9		90	5.4
10		100	6.0

Cinque valvole cardiache meccaniche bi-leaflet a confronto:

- **Sorin Overline** (Sorin Biomedica, Saluggia, Italy)
- **On-X** (Medical Carbon Research Institute, Austin, Texas)
- **CarboMedics Top Hat** (CarboMedics Inc, Austin, Texas)
- **St. Jude Regent** (St. Jude Medical, St. Paul, Minnesota)
- **Medtronic Advantage** (Medtronic, Minneapolis, Texas)



spettri della valvola On-X a SV 50 (sx) e SV 60 (dx)



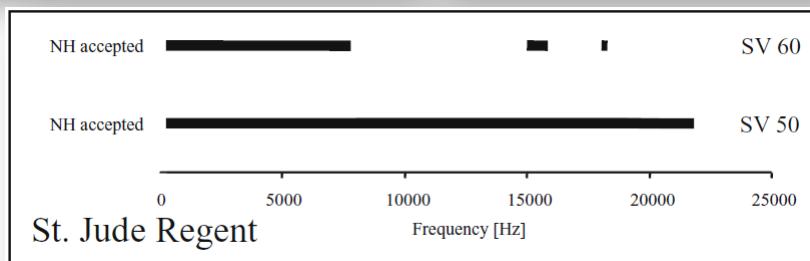
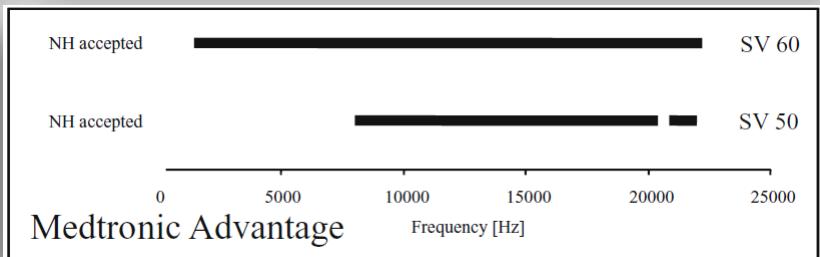
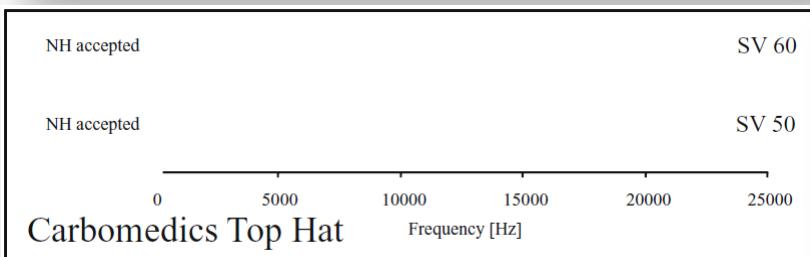
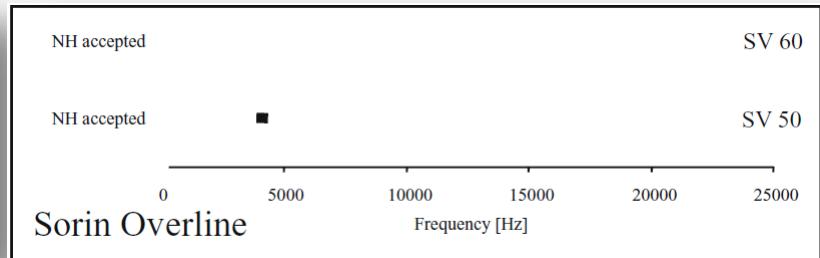
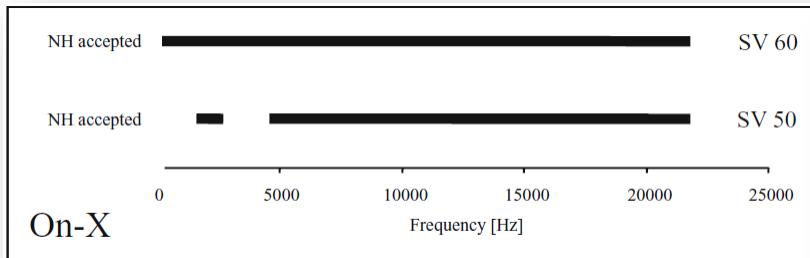
spettri della valvola St Jude a SV 50 (sx) e SV 60 (dx)

#	On-X		CarboMedics Top Hat		Sorin OverLine		Medtronic Advantage		St. Jude Regent	
	Frequency (Hz)	Amplitude (au)	Frequency (Hz)	Amplitude (au)	Frequency (Hz)	Amplitude (au)	Frequency (Hz)	Amplitude (au)	Frequency (Hz)	Amplitude (au)
1	12 059 ± 71	47.33 ± 3.03	12 016 ± 50	31.97 ± 3.08	12 059 ± 244	32.97 ± 2.11	17 421 ± 82	15.01 ± 5.39	17 356 ± 50	34.74 ± 7.64
2	12 102 ± 111	49.61 ± 5.25	11 972 ± 71	48.70 ± 4.71	12 209 ± 394	39.36 ± 2.38	17 485 ± 0	17.02 ± 2.81	17 270 ± 50	30.86 ± 7.91
3	12 059 ± 122	71.11 ± 2.66	12 016 ± 50	63.54 ± 1.59	12 231 ± 70	48.51 ± 3.85	17 528 ± 50	14.81 ± 3.16	17 249 ± 43	26.62 ± 5.82
4	12 016 ± 87	47.31 ± 7.66	11 951 ± 43	71.85 ± 2.89	12 231 ± 70	53.95 ± 5.96	17 485 ± 0	16.94 ± 2.93	17 249 ± 43	36.06 ± 6.02
5	11 908 ± 43	61.26 ± 17.64	11 994 ± 83	81.90 ± 9.27	12 274 ± 149	57.31 ± 11.02	17 528 ± 50	17.71 ± 5.60	17 249 ± 43	34.42 ± 2.87
6	12 382 ± 257	22.68 ± 3.42	11 822 ± 43	60.08 ± 3.54	12 231 ± 70	22.48 ± 0.75	17 657 ± 122	12.77 ± 4.34	17 227 ± 0	27.06 ± 3.03
7	12 488 ± 252	27.71 ± 2.53	11 951 ± 83	55.49 ± 4.32	12 145 ± 70	31.65 ± 1.73	17 464 ± 43	14.40 ± 6.01	17 249 ± 43	25.14 ± 5.34
8	12 425 ± 163	31.56 ± 5.89	11 865 ± 43	76.22 ± 5.72	12 145 ± 99	37.95 ± 2.60	17 550 ± 43	16.58 ± 5.37	17 249 ± 43	31.68 ± 4.01
9	12 317 ± 244	37.88 ± 8.01	11 843 ± 50	109.87 ± 2.98	12 145 ± 70	43.57 ± 4.50	17 614 ± 149	17.96 ± 3.74	17 270 ± 50	36.77 ± 5.19
10	12 016 ± 112	30.93 ± 3.22	11 779 ± 43	142.56 ± 7.24	12 403 ± 222	49.58 ± 6.64	17 291 ± 147	16.84 ± 2.41	17 227 ± 0	40.43 ± 3.92

Data are mean ± SD

au, arbitrary units

dati caratteristici degli spettri



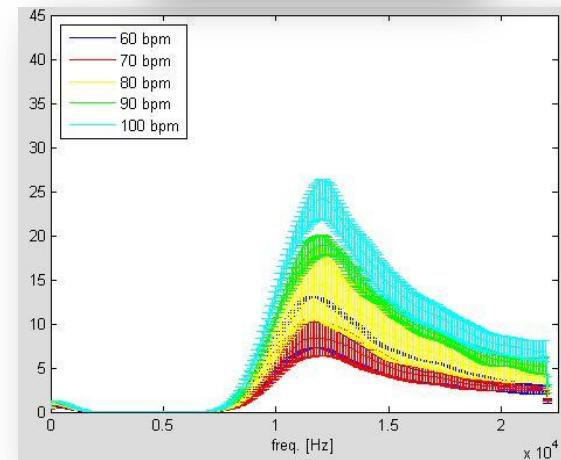
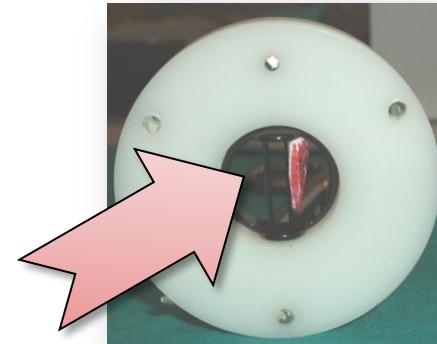
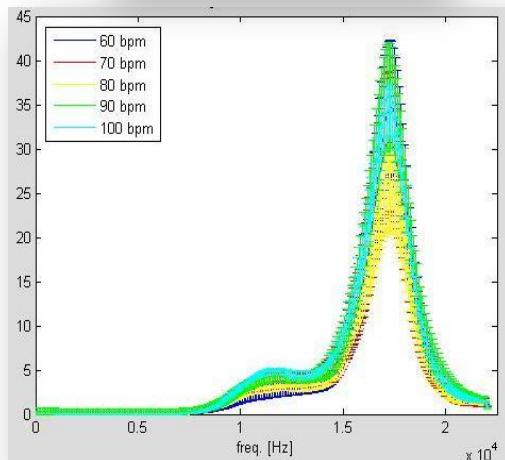
analisi statistica sulla “riproducibilità” del suono

ORIGINAL ARTICLE

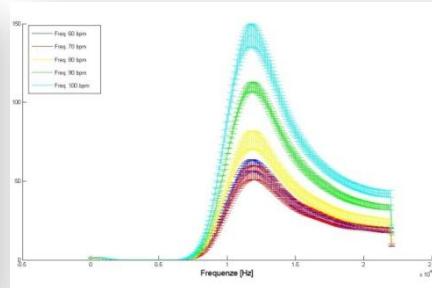
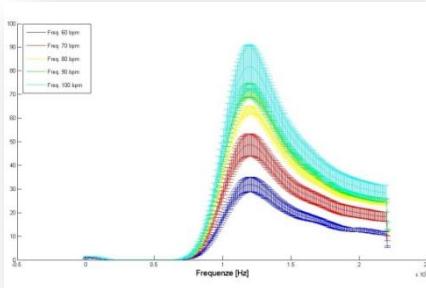
**Andrea Bagno, PhD · Federico Anzil, BS
Roberto Buselli, MS · Elena Pesavento, MS
Vincenzo Tarzia, MD · Vittorio Pengo, MD
Tomaso Bottio, MD · Gino Gerosa, MD**

Bileaflet mechanical heart valve closing sounds: in vitro classification by phonocardiographic analysis

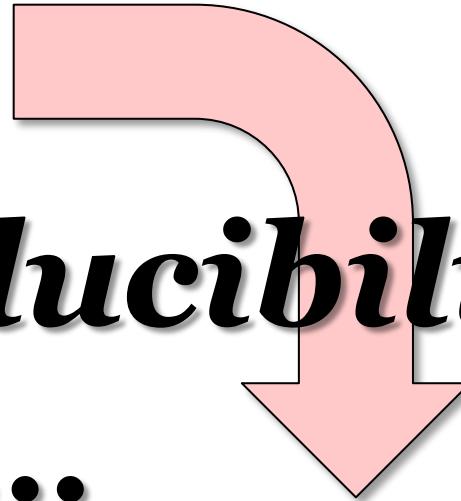




spettri della valvola St Jude senza (sx) e con trombo (dx)



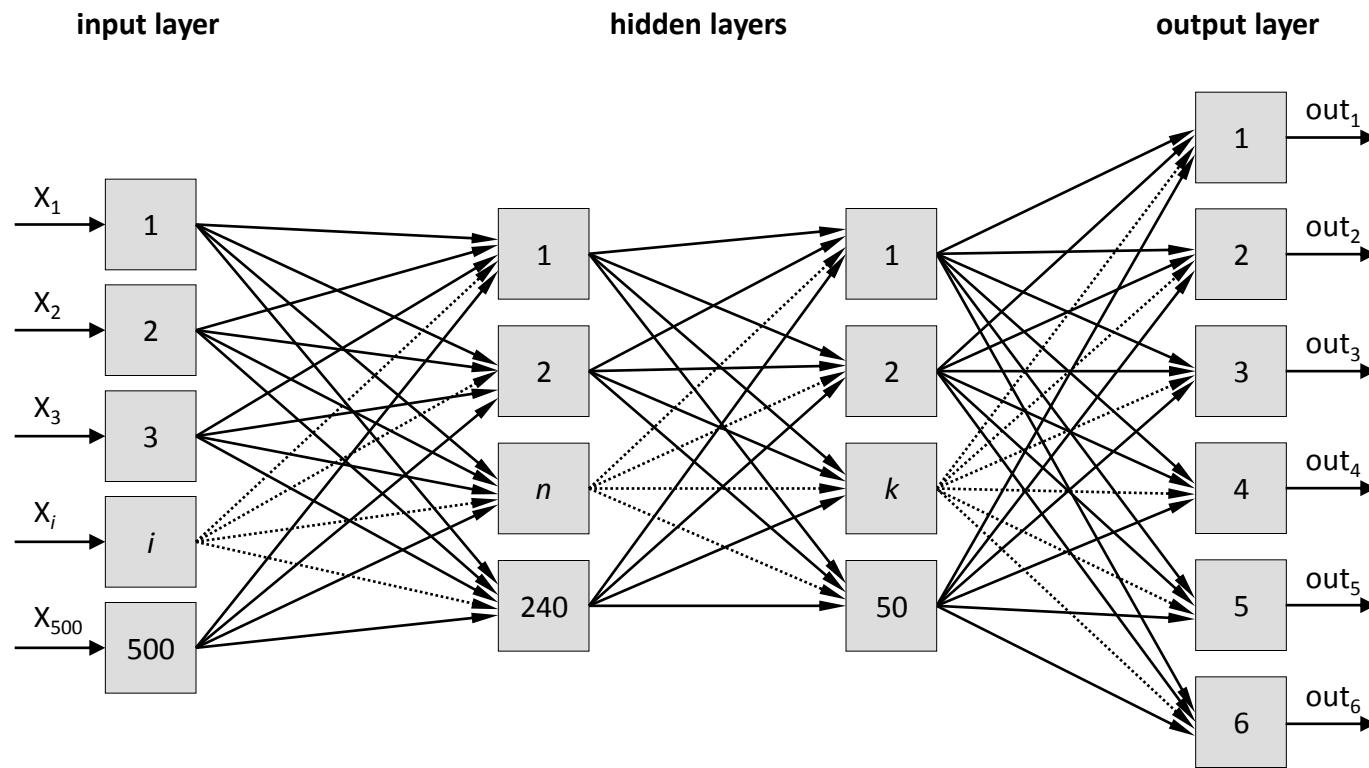
*... dalla riproducibilità
alla diagnosi ...*



RETI NEURALI ARTIFICIALI

- strumenti matematici formati da unità computazionali (neuroni) raggruppati in strati e connessi tra di loro
- i pesi delle connessioni vengono modificati attraverso un processo di addestramento (training)
- le reti feed-forward multistrato consentono la risoluzione di problemi di riconoscimento di pattern e classificazione





esempio di rete neurale artificiale

La rete neurale, dopo essere stata opportunamente addestrata con una serie di spettri venendo “forzata” ad attribuire ogni spettro alla classe corrispondente, è in grado di classificare spettri incogniti (*mai visti prima*)

La rete genera in uscita un valore numerico tra 0 e 1:
→ tanto più il valore è vicino a 1, tanto più la rete associa lo spettro in esame alla classe corrispondente
→ tanto più il valore è vicino a 0, tanto meno la rete associa lo spettro in esame alla classe corrispondente

la rete neurale artificiale è stata addestrata a riconoscere queste classi

Carbomedics

St Jude Regent

Sorin Overline

On-X

Medtronic Advantage

St Jude Regent con trombo

Medtronic Advantage con trombo

Carbomedics con trombo

Sorin Overline con trombo

On-X con trombo

quando alla rete si sottopone uno spettro (mai visto prima) della valvola St Jude con trombo, produce questi valori di output

Carbomedics	0,042
St Jude Regent	0,004
Sorin Overline	0,059
On-X	0,013
Medtronic Advantage	0,001
St Jude Regent con trombo	0,922
Medtronic Advantage con trombo	0,062
Carbomedics con trombo	0,060
Sorin Overline con trombo	0,076
On-X con trombo	0,023

... e quindi prende questa decisione, attribuendo lo spettro alla classe corrispondente:

Carbomedics	0,042	0
St Jude Regent	0,004	0
Sorin Overline	0,059	0
On-X	0,013	0
Medtronic Advantage	0,001	0
St Jude Regent con trombo	0,922	1
Medtronic Advantage con trombo	0,062	0
Carbomedics con trombo	0,060	0
Sorin Overline con trombo	0,076	0
On-X con trombo	0,023	0

Phonocardiographic Classification of Mechanical Heart Valves Using Artificial Neural Networks

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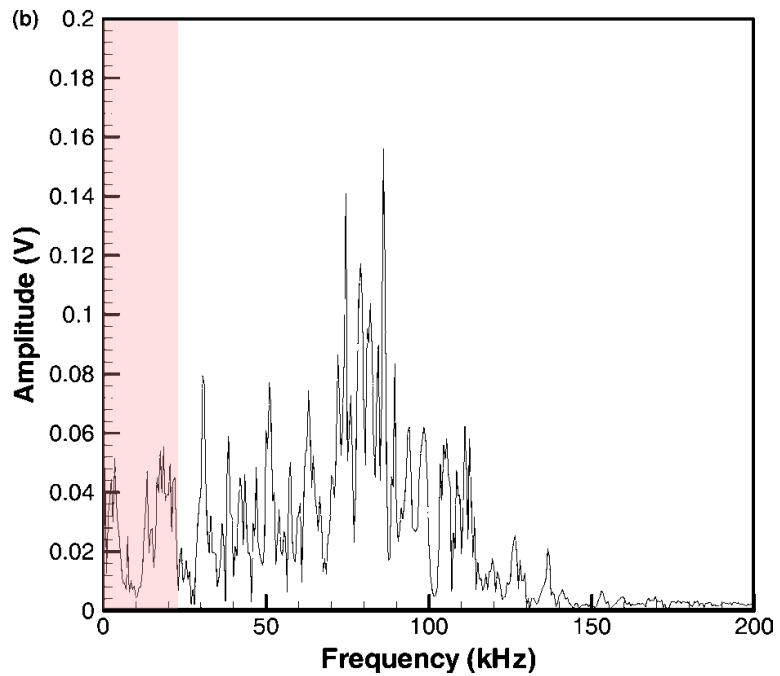
³ Clinical Cardiology, Department of Cardiologic, Thoracic and Vascular Sciences, University of Padova Medical School, Padova, Italy

O. Dössel and W.C. Schlegel (Eds.): WC 2009, IFMBE Proceedings 25/VII, pp. 110–113, 2009.
www.springerlink.com



*... dall'udibile
all'ultrasuono ...*



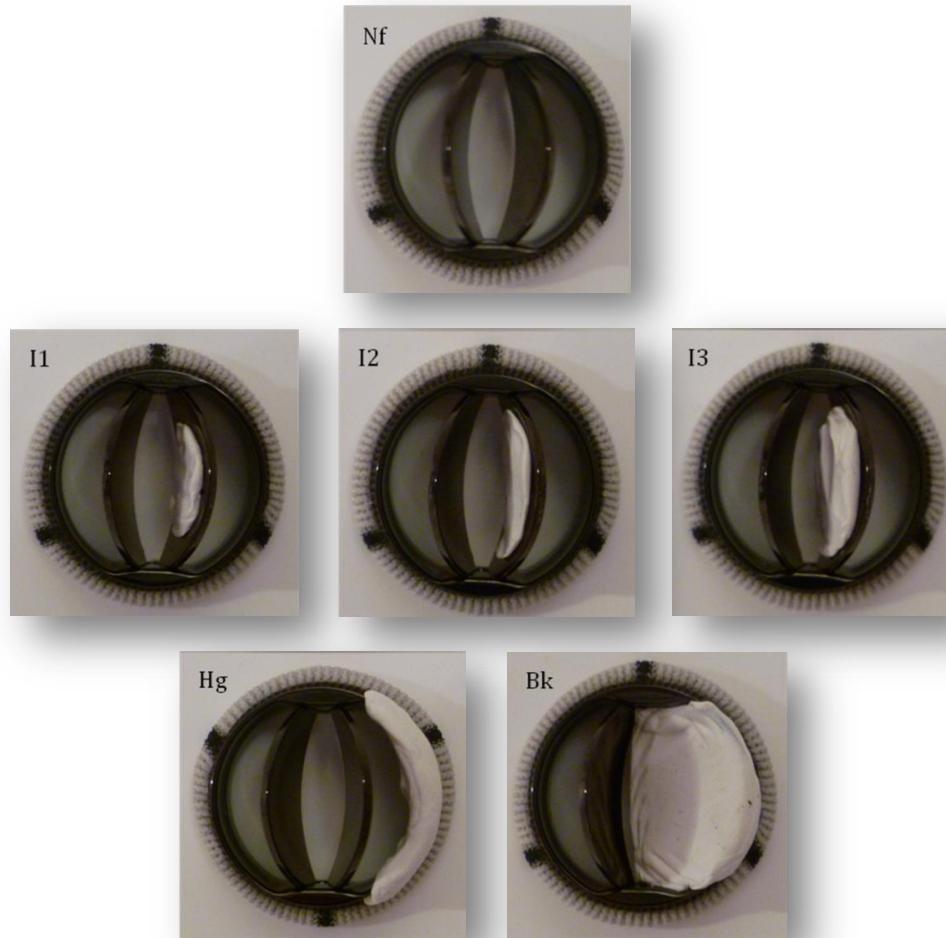


On the Closing Sounds of a Mechanical Heart Valve

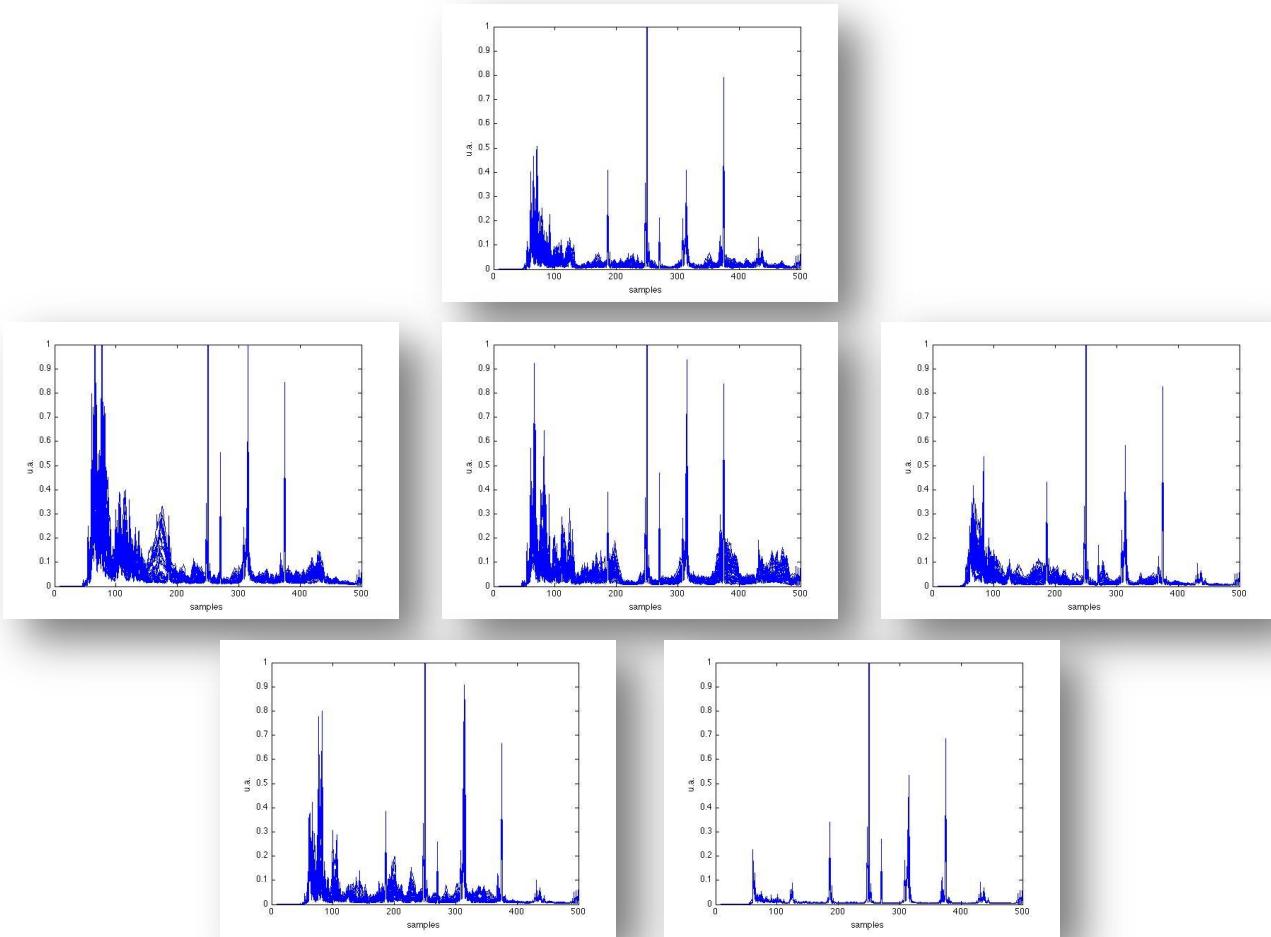
CHANGFU WU,¹ BRUCE A. HERMAN,² STEPHEN M. RETTA,² LAURENCE W. GROSSMAN,²
JIA-SHING LIU,³ and NED H. C. HWANG³

Annals of Biomedical Engineering, Vol. 33, No. 6, June 2005 (© 2005) pp. 743–750

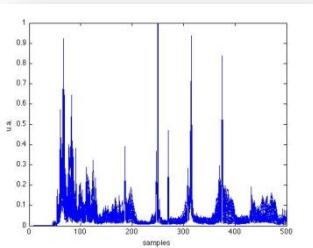
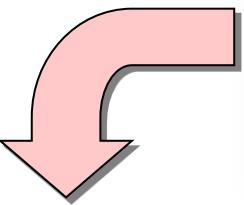
- 1) Nf** normofunzionante (pulita)
- 2) I₁** formazione di panno da 0,07 g
- 3) I₂** formazione di panno da 0,15 g
- 4) I₃** formazione di panno da 0,36 g
- 5) Hg** trombo da 0,29 g
- 6) Bk** emidisco bloccato con trombo da 0,75 g



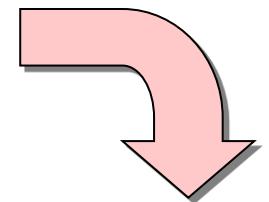
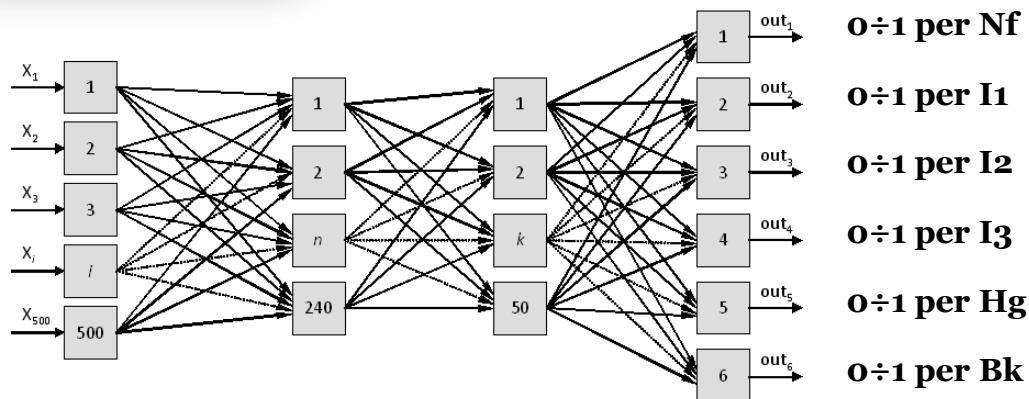
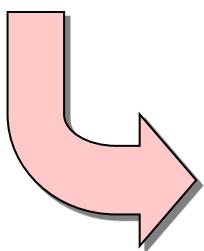
le 6 classi funzionali considerate



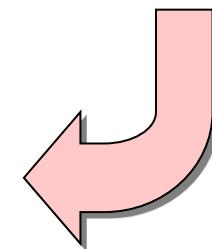
gli spettri calcolati dai suoni delle diverse classi funzionali



- ogni spettro viene suddiviso in 500 campioni
- $(x_1, \dots x_{500})$ è il vettore di input



la rete calcola 6 valore di output (da 0 a 1) per ciascuna classe funzionale



INPUT
Nf

		OUTPUT				
	Nf	I1	I2	I3	Hg	Bk
SV50BR60	0.9107	0.0117	0.0114	0.0104	0.0297	0.0822
	0.8730	0.0125	0.0101	0.0300	0.0341	0.0183
	0.9839	0.0184	0.0188	0.0145	0.0088	0.0004
	0.9856	0.0127	0.0032	0.0216	0.0168	0.0003
	0.9864	0.0261	0.0094	0.0253	0.0053	0
	0.9708	0.0047	0.0060	0.0392	0.0372	0.0021
	0.9959	0.0262	0.0089	0.0101	0.0050	0.0002
	0.9920	0.0120	0.0105	0.0141	0.0037	0
	0.9876	0.0142	0.0043	0.0674	0.0038	0.0001
	0.9864	0.0261	0.0094	0.0253	0.0053	0

INPUT
I₁

	Nf	I ₁	I ₂	I ₃	Hg	Bk
SV50BR60	0.0232	0.8949	0.0083	0.0326	0.0474	0.0002
SV50BR70	0.0075	0.9658	0.0083	0.0100	0.0499	0
SV50BR80	0.0046	0.9820	0.0230	0.0528	0.0031	0
SV50BR90	0.0021	0.9740	0.0111	0.0204	0.0096	0
SV50BR100	0.0017	0.9844	0.0102	0.0234	0.0039	0
SV60BR60	0.0293	0.9815	0.0025	0.0477	0.0157	0.0002
SV60BR70	0.0269	0.9907	0.0035	0.0119	0.0029	0
SV60BR80	0.0079	0.9898	0.0064	0.0106	0.0050	0
SV60BR90	0.0034	0.9654	0.0340	0.0035	0.0214	0
SV60BR100	0.0017	0.9844	0.0101	0.0234	0.0039	0

OUTPUT

INPUT
I₂

		OUTPUT					
		Nf	I₁	I₂	I₃	Hg	Bk
SV50BR60	0.0501	0.0200	0.8347	0.0066	0.0244	0.0039	
	0.0076	0.0171	0.9778	0.0037	0.0158	0.0021	
	0.0034	0.0120	0.9872	0.0006	0.0288	0.0007	
	0.0133	0.0380	0.9781	0.0015	0.0037	0.0012	
	0.0060	0.0050	0.9942	0.0007	0.0022	0.0011	
	0.0047	0.0103	0.9916	0.0011	0.0081	0.0010	
	0.0138	0.0037	0.9945	0.0006	0.0019	0.0037	
	0.0028	0.0217	0.9914	0.0003	0.0036	0.0017	
	0.0010	0.0068	0.9940	0.0004	0.0025	0.0018	
	0.0060	0.0050	0.9942	0.0007	0.0022	0.0011	

INPUT
I₃

	OUTPUT					
	Nf	I₁	I₂	I₃	Hg	Bk
SV50BR60	0.0117	0.0162	0.0071	0.9048	0.0181	0.0276
SV50BR70	0.0308	0.0050	0.0052	0.9222	0.0206	0.0045
SV50BR80	0.0051	0.0156	0.0027	0.9832	0.0170	0.0008
SV50BR90	0.0087	0.0181	0.0021	0.9956	0.0057	0.0006
SV50BR100	0.0006	0.0046	0.0088	0.9934	0.0310	0.0001
SV60BR60	0.0403	0.0039	0.0031	0.9379	0.0200	0.0084
SV60BR70	0.0261	0.0030	0.0011	0.9911	0.0389	0.0004
SV60BR80	0.0111	0.0024	0.0028	0.9893	0.0270	0.0002
SV60BR90	0.0083	0.0048	0.0074	0.9906	0.0128	0.0001
SV60BR100	0.0006	0.0046	0.0088	0.9934	0.0310	0.0001

INPUT
Hg

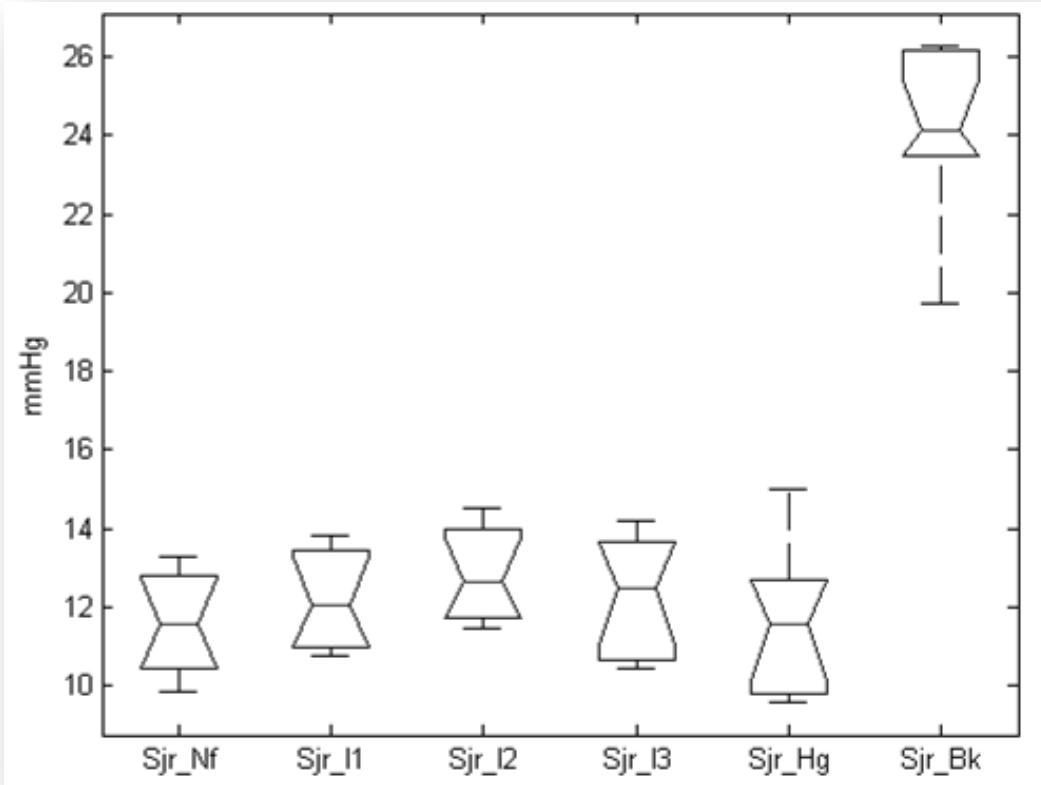
OUTPUT

Nf **I1** **I2** **I3** **Hg** **Bk**

SV50BR60	0.0284	0.0068	0.0042	0.0240	0.8701	0.0423
SV50BR70	0.0031	0.0021	0.0124	0.0075	0.9943	0.0021
SV50BR80	0.0016	0.0215	0.0193	0	0.9989	0.0129
SV50BR90	0.0004	0.0279	0.0025	0.0003	0.9988	0.0091
SV50BR100	0.0006	0.0064	0.0013	0.0096	0.9619	0.0005
SV60BR60	0.0029	0.0053	0.0201	0.0025	0.9923	0.0070
SV60BR70	0.0142	0.0084	0.0173	0.0004	0.9846	0.0011
SV60BR80	0.0003	0.0015	0.0029	0.0302	0.9821	0.0004
SV60BR90	0.0003	0.0107	0.0273	0.0006	0.9989	0.0077
SV60BR100	0.0022	0.0106	0.0024	0.0129	0.9907	0.0010

**INPUT
Bk**

	OUTPUT					
	Nf	I1	I2	I3	Hg	Bk
SV50BR60	0.0987	0.0058	0.0128	0.0390	0.0232	0.9189
SV50BR70	0.0342	0.0095	0.0189	0.1122	0.0101	0.8833
SV50BR80	0.0162	0.0060	0.0136	0.1717	0.0291	0.8831
SV50BR90	0.0244	0.0038	0.0247	0.0304	0.0342	0.9695
SV50BR100	0.0444	0.0065	0.0102	0.0620	0.0160	0.9392
SV60BR60	0.0770	0.0047	0.0147	0.0421	0.0235	0.9344
SV60BR70	0.0418	0.0028	0.0228	0.0207	0.0266	0.9678
SV60BR80	0.0213	0.0028	0.0518	0.0184	0.0445	0.9509
SV60BR90	0.0452	0.0063	0.0104	0.0728	0.0258	0.9108
SV60BR100	0.0332	0.0034	0.0204	0.0290	0.0280	0.9718



Comparative classification of thrombotic formations on bileaflet mechanical heart valves by phonographic analysis

Clemens Romata · Francesca Maria Susin ·
Andrea Cambi · Vincenzo Tarzia · Vittorio Pengo ·
Gino Gerosa · Andrea Bagno

In-Vitro Detection of Thrombotic Formation on Bileaflet Mechanical Heart Valves

Francesca Maria Susin¹, Vincenzo Tarzia², Tomaso Bottio², Vittorio Pengo⁴, Andrea Bagno³, Gino Gerosa²

The Journal of Heart Valve Disease 2011;20:

Applicazione della rete neurale ai segnali acquisiti *in vivo* su 30 portatori di valvola cardiaca meccanica bi-leaflet :

- ✓ 1 paziente attribuito alla condizione *Nf*
- ✓ 15 pazienti attribuiti alla condizione *I1*
- ✓ 0 pazienti attribuiti alla condizione *I2*
- ✓ 11 pazienti attribuiti alla condizione *I3*
- ✓ 0 pazienti attribuiti alla condizione *Hg*
- ✓ 3 pazienti attribuiti alla condizione *Bk*

3 pazienti risultano avere un *leaflet* completamente bloccato → **diagnosi smentita dal quadro clinico**

26 pazienti risultano appartenere alle condizioni intermedie I_1 e I_3 → **diagnosi compatibile con il quadro clinico**



Valvole cardiache ingegnerizzate (TEHVs)

Definizione ①:

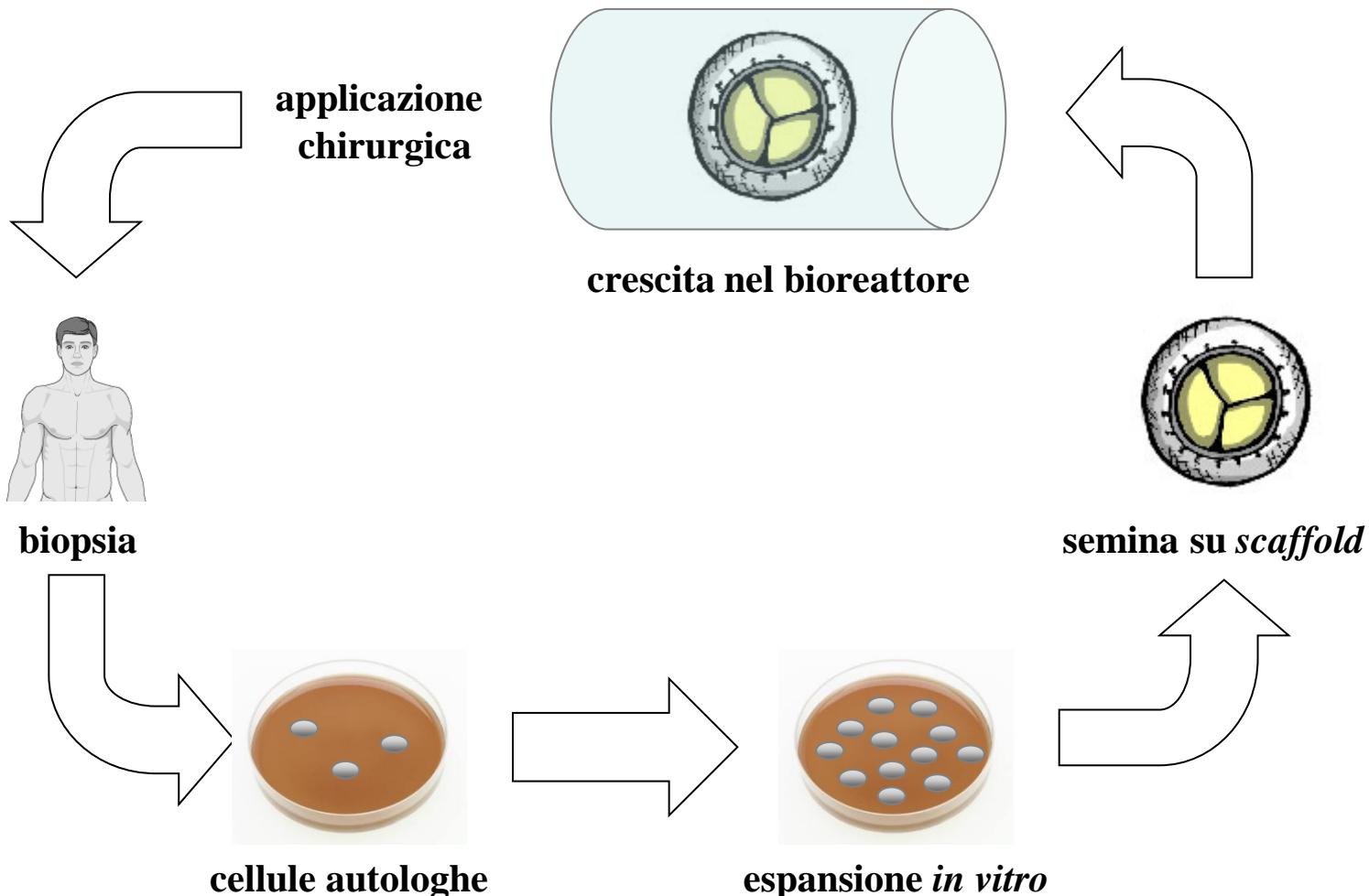
l'ingegneria dei tessuti rappresenta l'uso combinato di cellule, materiali di supporto e fattori biochimici allo scopo di migliorare e/o sostituire una o più funzioni biologiche

Definizione ②:

la medicina rigenerativa rappresenta un nuovo approccio terapeutico finalizzato alla rigenerazione biologica di un tessuto anziché alla sua sostituzione

Secondo Langer e Vacanti¹ l'ingegneria dei tessuti è "an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve tissue function or a whole organ"

1. Langer and Vacanti. Tissue engineering. Science 260,920;1993.





valvola aortica ingegnerizzata

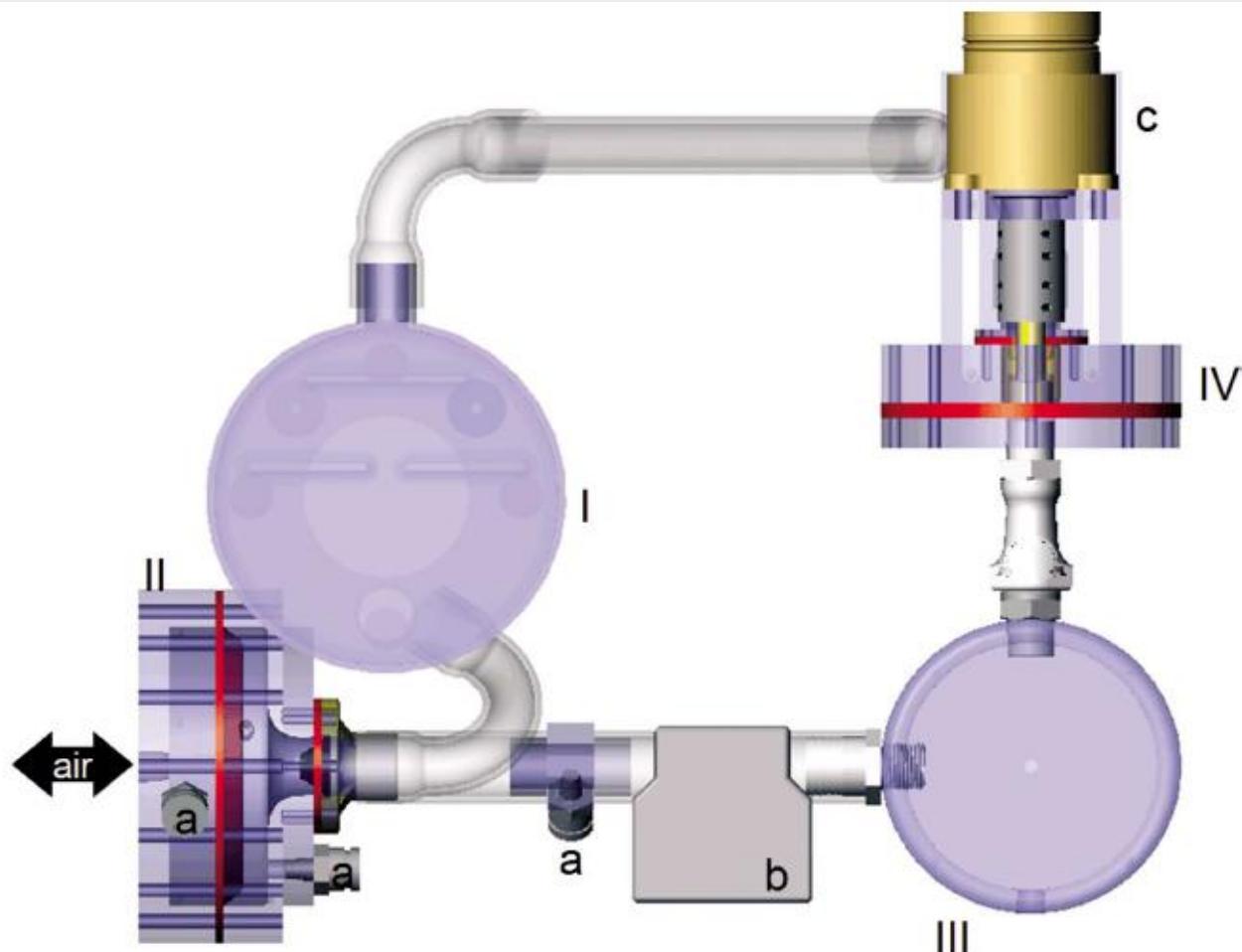


FIGURE 1. Overhead diagram of system: atrium (I), ventricle (II), compliance chamber (III), variable resistor (IV), pressure sensors (a), flow sensor (b), stepper motor (c).



FIGURE 2. Photograph of the functioning flow system within the incubator. Compound identification same as in Fig. 1.

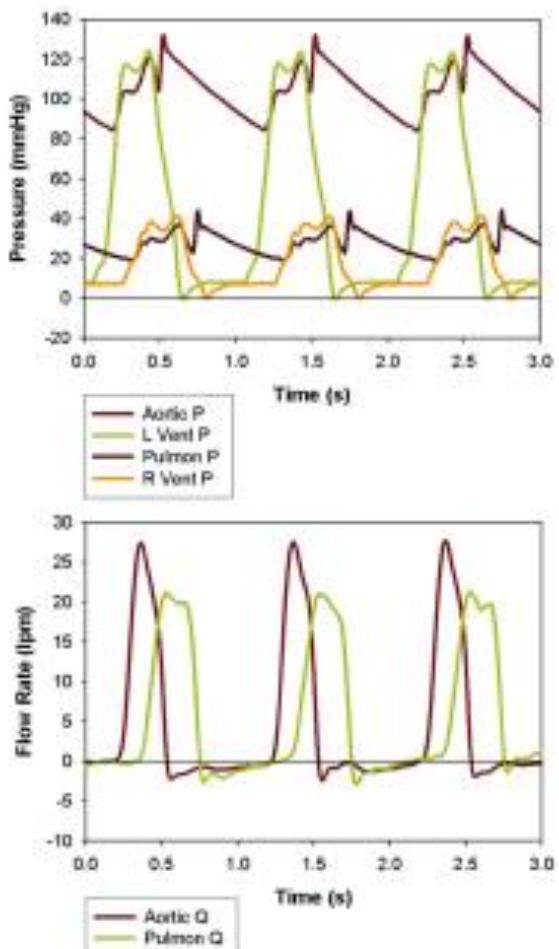


FIGURE 7. Acquired physiologic waveforms at 60 bpm: pressure (mmHg) and volumetric flow (l pm).

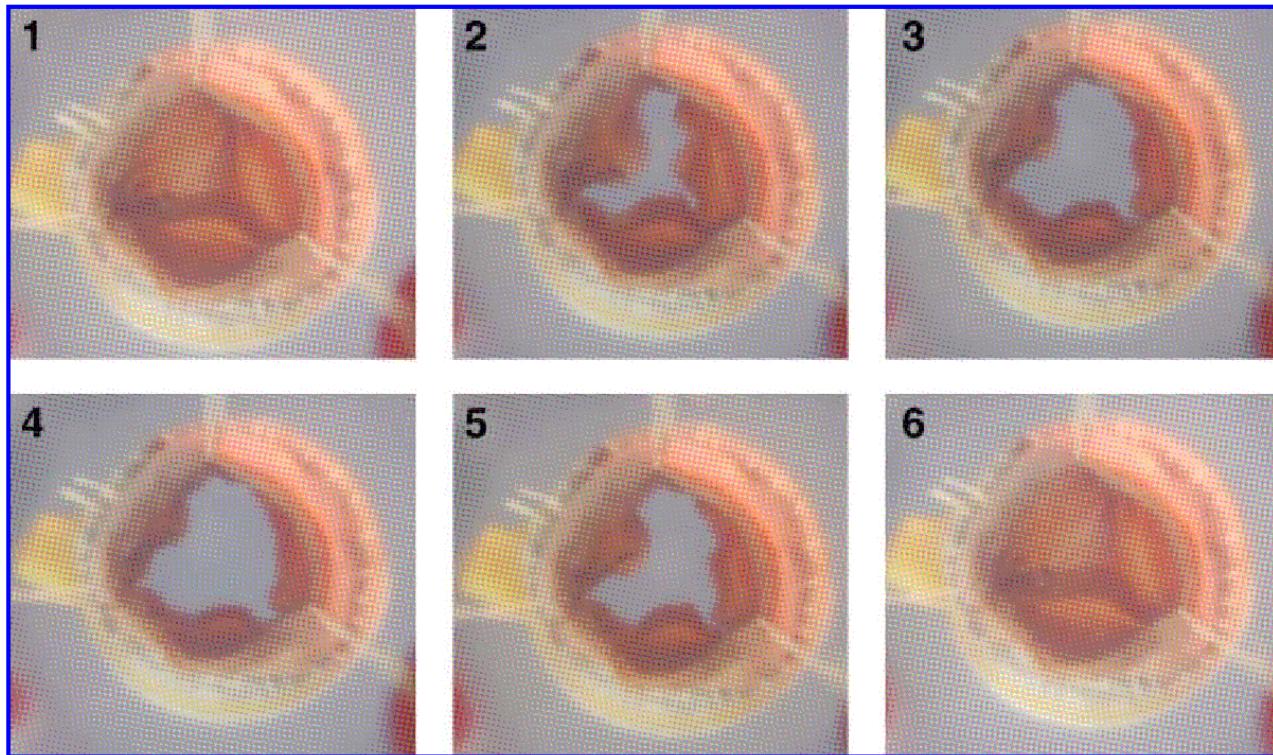
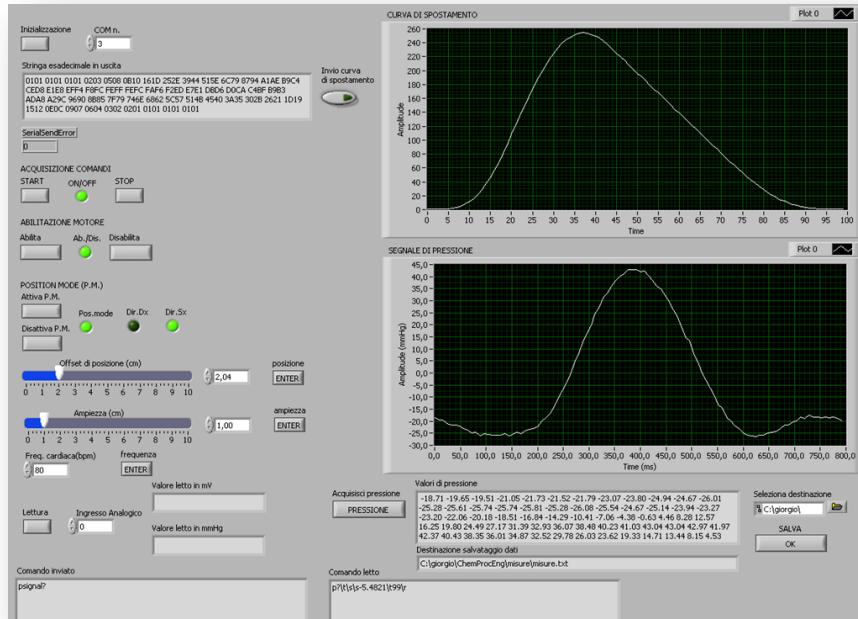
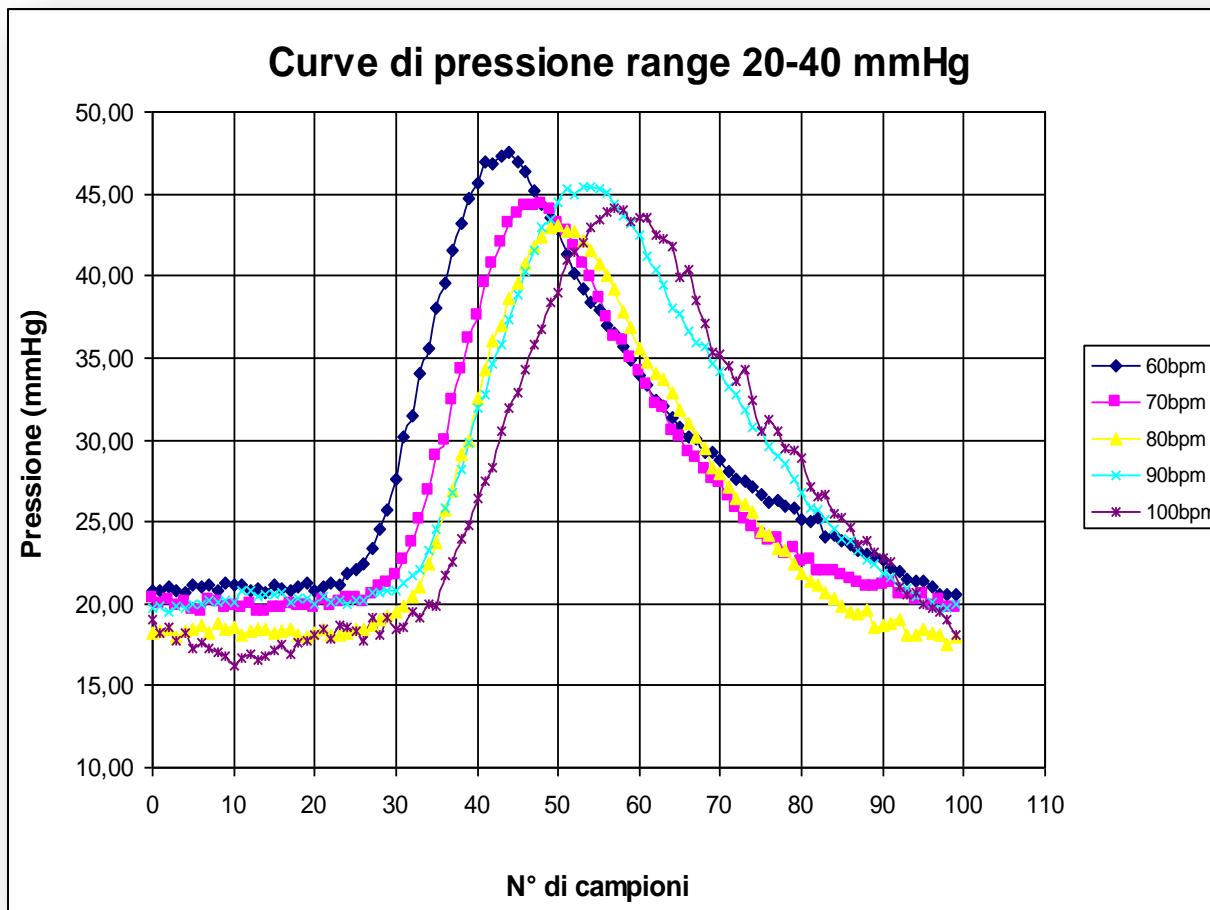
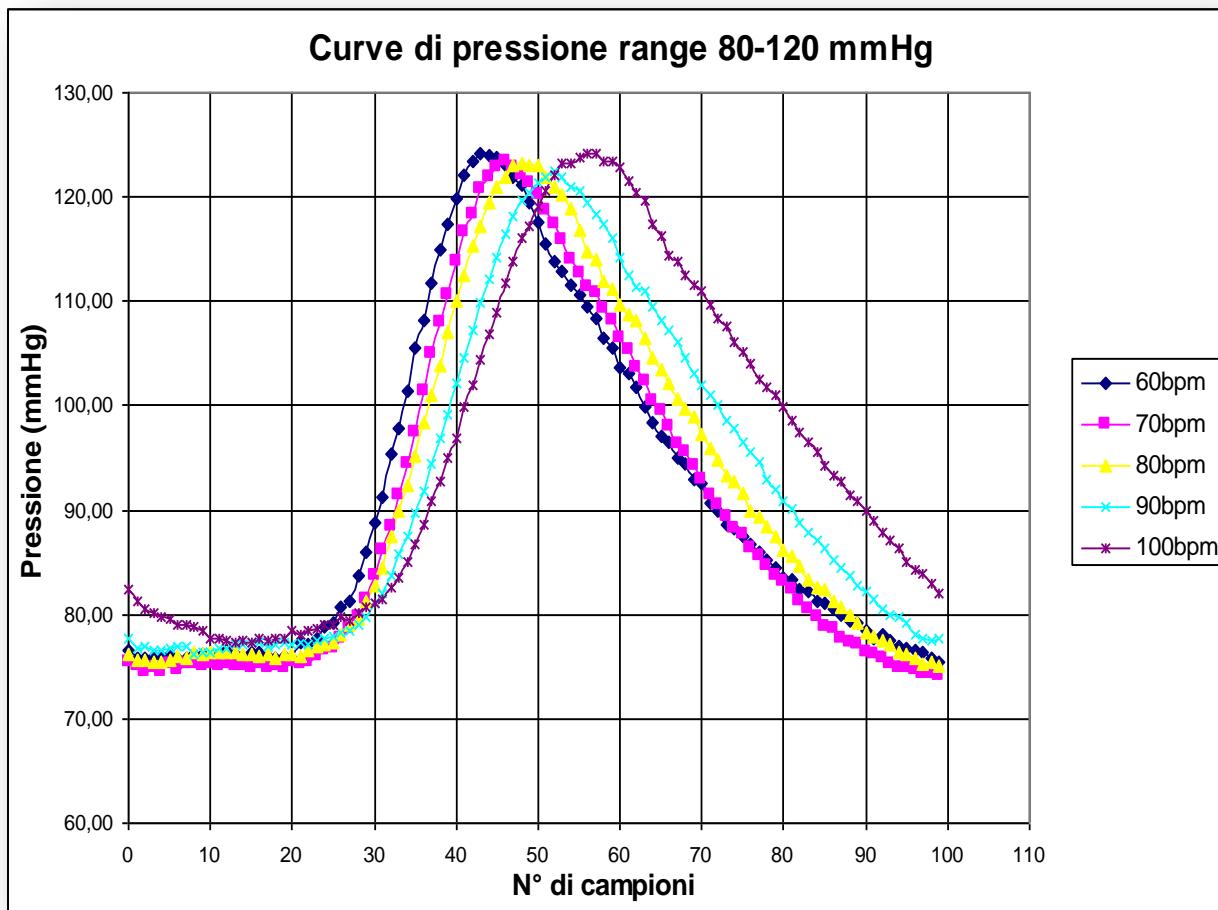
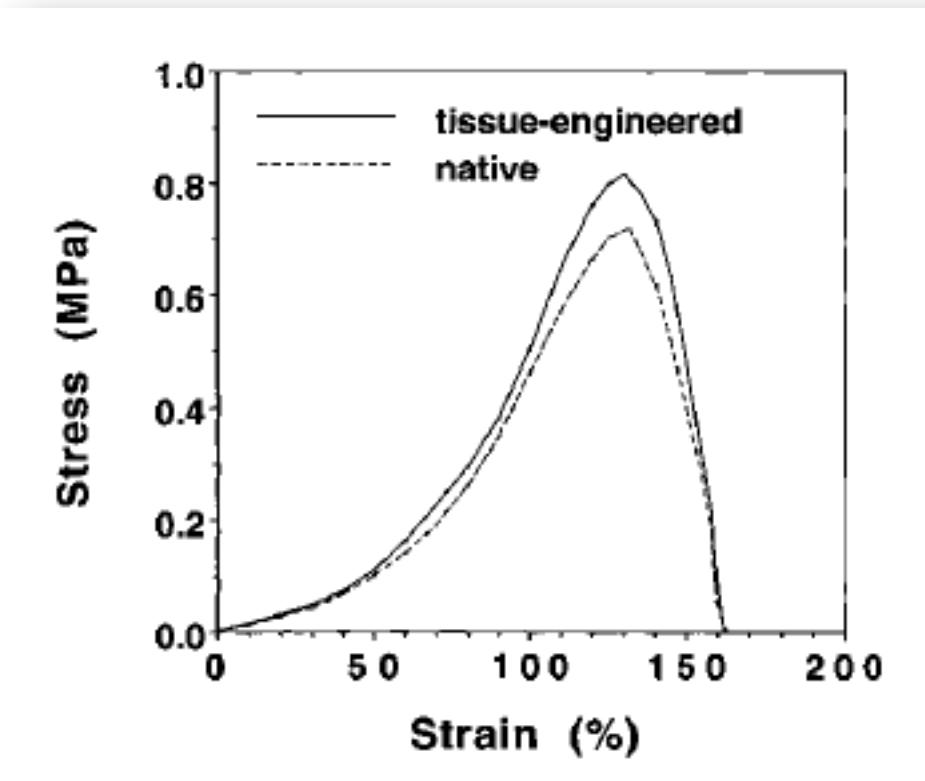


FIG. 2. Sequential images showing valve opening and closing in the bioreactor. Medium is removed for enhanced observation. Color images available online at www.liebertonline.com/ten.











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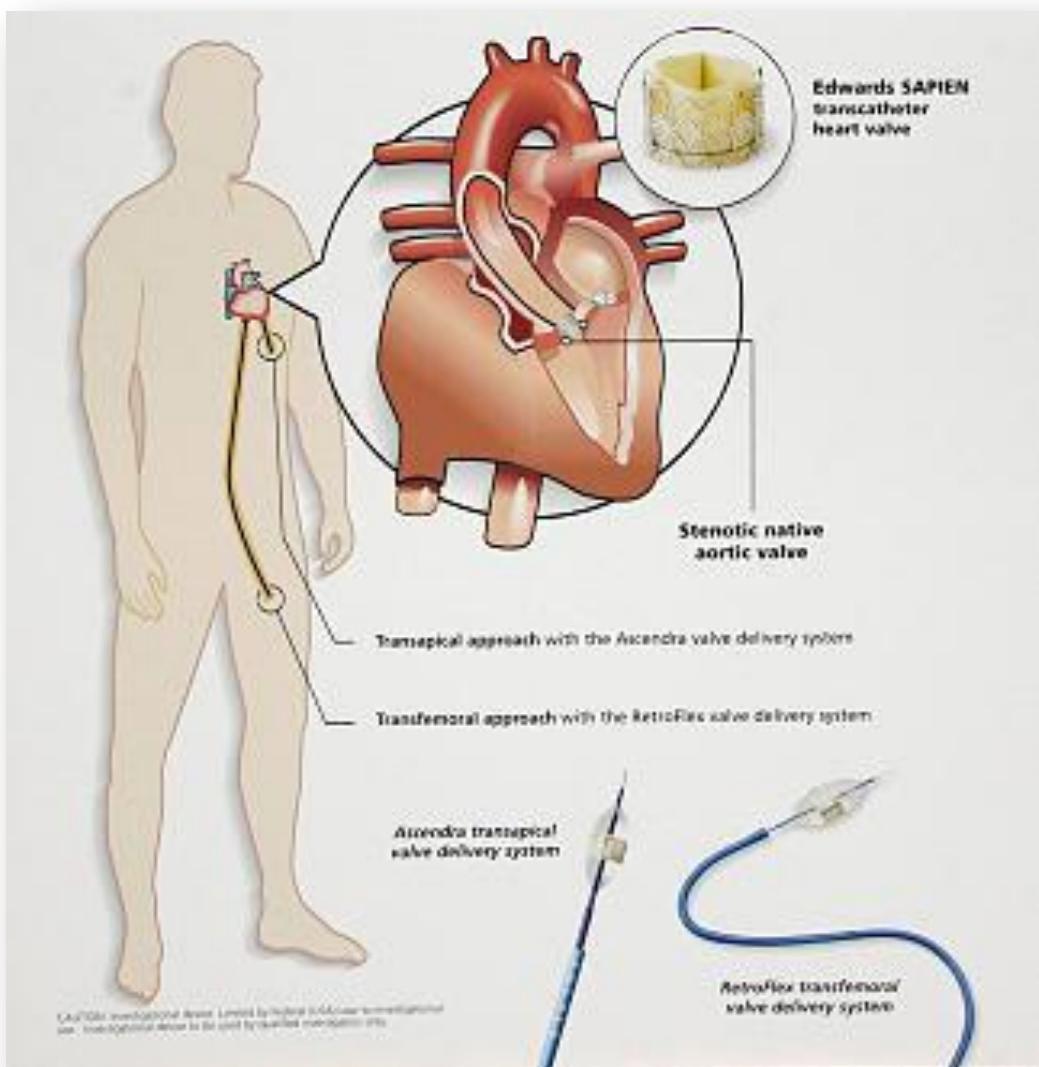
Review

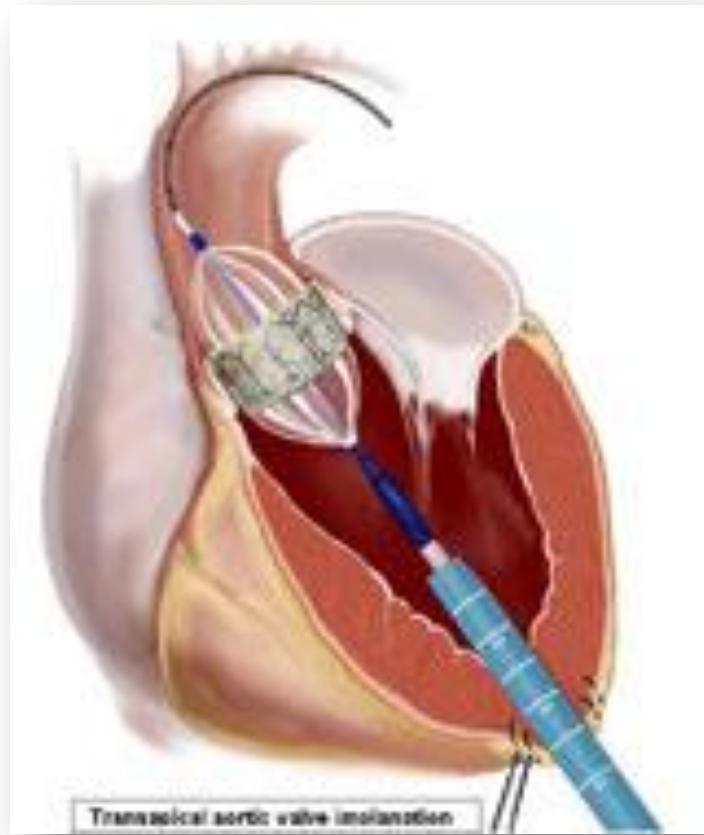
Cells, scaffolds and bioreactors for tissue-engineered heart valves: a journey from basic concepts to contemporary developmental innovations[☆]

Alessandro Gandaglia ^{a,*}, Andrea Bagno ^b, Filippo Naso ^a, Michele Spina ^c, Gino Gerosa ^a



Valvole cardiache transcutanee





impianto transapicale di valvola aortica

