ISTITUTO SUPERIORE DI SANITÀ

2nd Workshop

BIOFLUMEN
Biological Fluid Mechanics Network

Istituto Superiore di Sanità
Rome, 15 April 2002

ABSTRACT BOOK

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The incidence of pathologies of the circulatory system in the developed countries urgently points out the necessity of studying the phenomena associated with the physiopathological functioning of the circulatory system, paying attention to both the strictly fluid dynamical aspect and the interaction between blood and the circulatory districts. The 2nd BioFluMeN (Biological Fluid Mechanics Network) Workshop aims at comparing the different experiences at national level in continuity with the results of the 1st Workshop held at the Istituto Superiore di Sanità (Italian National Institute of Health) in 2000.

Key words: Models of the circulatory system, Fluid dynamics, Implantable devices

Istituto Superiore di Sanità
A cura di Mauro Grigioni e Gianni Pedrizzetti
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L’incidenza delle malattie del sistema cardiocircolatorio nei paesi sviluppati rende particolarmente urgente lo sforzo di studiare l’insieme dei fenomeni connessi al funzionamento fisiopatologico del sistema circolatorio, sia relativamente all’aspetto strettamente fluidodinamico, sia riguardo all’interazione fra il sangue e i vari distretti circolatori. Il 2° Workshop BioFluMeN (Biological Fluid Mechanics Network) intende costituire uno spazio di riflessione e confronto aperto a tutti i gruppi nazionali interessati a queste tematiche, continuando l’esperienza del 1° Workshop tenutosi presso l’Istituto Superiore di Sanità nel 2000.

Parole chiave: Modelli del sistema circolatorio, Fluidodinamica, Dispositivi impiantabili

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# TABLE OF CONTENTS

Preface ........................................................................................................................................ iii

Programme .................................................................................................................................... v

First session
    Institutional work ..................................................................................................................... 1

Second session
    Collaborations ....................................................................................................................... 49

Authors’ index ............................................................................................................................. 71
The pathologies of the circulatory system represent one of the most important causes of morbidity and mortality in developed countries; on account of higher level of life expectancy, the consideration of biomechanical issues – related to the diseases characterized by progressive dysfunctions of organs and/or tissues – becomes even more important. In this framework, efforts are particularly necessary to study the phenomena related to the physiopathological function of the circulatory system, paying attention to both the strictly fluid dynamical aspect and the interaction between blood pumping action and the impedances of circulatory districts, in which the prosthetic devices (heart supports, cardiac valves, vascular prostheses, stents) must be implanted. In fact prosthetic devices have become by now essential tools in the clinical praxis, nevertheless, they also occasionally proved to be potentially associated to many complications (e.g. thromboembolism, hemolysis, failures, etc.) of which the fluid dynamics and bio mechanics of both the device itself and the heart-arterial tree system are the primary causes.

The 2nd BioFluMeN Workshop, which follows the first meeting also held at the Istituto Superiore di Sanità in 2000, is meant to be the expression of the need of comparing the experiences at national level in the field of the research in bioengineering and, to be more precise, of that part of the research in bioengineering which deals with the modelling and the study of the circulatory system. As was clearly seen during the 1st Workshop, the research efforts in this field have many different origins: besides university groups pertaining to engineering faculties, there are numerous groups originating from the field of mathematics, as well as cardiologists and cardiac surgeons who develop a quantitative approach to the solution of the problems posed daily by the clinical experience.

I have the pleasure to remember that the aim of this community concerns with the stimulus to use updated biomechanical knowledge in clinics for significant improvements of the patient’s quality of life. At the origin of the birth of BioFluMeN, or “Biological Fluid Mechanics Network”, we have tried to create a network for the exchange of experiences and information, useful to researchers already active in this field or simply interested in giving, in perspective, their contribution. Even though we do not have any intention to coordinate the already existing national activities in the field of bioengineering, BioFluMeN intends to be an occasion of comparison and discussion open to all the interested researchers in biomechanics and haemodynamics, without the ambition of substituting itself to existing institutions or organizations. Instead, it is meant as an horizontal occasion in which we can experiment new visions of the discipline. We are confident that this Workshop, as the 1st BioFluMeN meeting, will be useful to the development of new research collaborations in our field and to find a common feeling towards a continuous patient-oriented development.

We hope that the informal aspect of the scientific discussions, which characterized the previous occasion, will also be present during the next Workshop and help us in the discussion. In view a valuable meeting in Rome, we wish to thank in advance the participants to the 2nd BioFluMeN Workshop.

Mauro Grigioni
PROGRAMME

Monday, 15 April 2002

8.30 Registration

9.00 Welcome address by the President of the Istituto Superiore di Sanità
   E. Garaci

9.10 Presentation of the 2nd BioFluMeN Workshop
   M. Grigioni

First session
INSTITUTIONAL WORK
Chairman: M. Grigioni

9.30 Medical devices European directives - critical aspects
   V. Barbaro

9.45 Endovascular stents: safety issues
   M. Abbate

10.00 Computational study of intravascular stent mechanical behavior
    F. Auricchio

10.15 Coffee Break

10.45 Galerkin method for fluids in domains with elastic walls
    M. Padula

11.00 Velocity fields and propagation phenomena in the arterial system
    G. Pezzinga

11.15 Numerical study of blood dynamics in vascular access methods: venous cannulation
    U. Morbiducci

11.30 A computational model of flow in stented elastic artery
    A. Tortoriello

11.45 Modeling the Fluid Dynamics of the Left Heart
    F. Domenichini
12.00  A hydrodynamic problem relevant for human vitreous dynamics  
       R. Repetto  

12.15  St Jude HP bileaflet prostheses: a survey on the determination of the effective  
       orifice area and on the analysis of the pressure recovery in steady state conditions  
       C. Del Gaudio  

12.30  Discussion  

13.00  Lunch  

**Second session**  
**COLLABORATIONS**  
Chairman: G. Pedrizzetti  

15.00  Fractal dimensions analysis of experiments in fetal surgery  
       G. D’Avenio  

15.15  Real time contrast echo: the need of ventricular wall tracking to quantify the  
       regional perfusion  
       G. Tonti  

15.30  Lagrangian description of flow field through an aortic heart valve.  
       A. Balducci  

15.45  A boundary integral equation approach for fluid-wall interaction in arterial vessels  
       U. Iemma  

16.00  Prosthetic heart valves cause mechanical stress and hemolytic anaemia in patients  
       with hereditary erythrocyte membrane defects  
       P. Caprari  

16.15  A new method for the noninvasive quantification of heart valve regurgitation  
       G. D’Avenio  

16.30  Coffee break  

16.45  Research collaboration: free space for discussion  

17.30  New addresses for BioFluMeN Community  

18.00  End of workshop
First session
Institutional work

Chairman
Mauro Grigioni
EUROPEAN DIRECTIVES ON MEDICAL DEVICES: CRITICAL ASPECTS

Vincenzo Barbaro
Laboratorio di Ingegneria Biomedica, Istituto Superiore di Sanità, Roma

1. Critical aspects of the directives
The Medical Directives present three extremely important aspects:
   i) device classification,
   ii) clinical investigations, and
   iii) post-market vigilance.

2. Device classification
   The Directive 93/42/EEC classifies all MDs in four classes with the aim of adapting conformity assessment procedures to the potential risk posed by the devices. The classification is based on the use intended by the manufacturers:
   
   CLASS I: the least critical devices, i.e. most of non-active medical devices.
   CLASS IIa: active medical devices that do not interact with the body.
   CLASS IIb: active medical devices.
   CLASS III: the most critical active devices and a few non-active devices that assist the function of vital organs. This class also includes active implantable devices and related accessories regulated by Directive 90/385/EEC.

   This classification is implemented through 18 rules that contemplate intended use, invasiveness, length of application, purpose (diagnostic or therapeutic), power supply (active or not), and exchange of energy with the human body also in view of the hazards posed to the site of application.

3. Clinical investigations
   Clinical data are necessary to assess the conformity of innovative devices, their efficacy, normal conditions of use, and potential undesirable side effects.

   The purpose of clinical data is to provide clinical evidence of the compliance with the essential requirements. Clinical evidence is gained when a qualified expert is able to conclude that the examined medical device complies with the following requirements:
   
   1. When, used under the conditions and for the purposes intended by the manufacturer, the device will not compromise the clinical condition or the safety of patients, or the safety and health of users or, where applicable, other persons.
   2. Any risks that may be associated with their use constitute acceptable risks when weighed against the benefits to the patient and are compatible with a high level of protection of health and safety.
The clinical evidence must be based on either a compilation of the relevant scientific literature currently available on the intended purpose of the device, or the results of the clinical investigations.

Any specific study in human subjects undertaken to verify the safety and performance of a specific medical device under normal conditions of use is defined as “Clinical Investigation” where “safety” is freedom of unacceptable risk of harm.

The need to perform clinical investigation results from the following considerations:
1. where a completely new device is proposed for the market, whose components, features and/or method of action are previously unknown;
2. where an existing device is modified and the modification might significantly affect the clinical safety and performance;
3. where a previously established device is proposed for a new indication.
4. where a device incorporates new materials, previously unknown, coming into contact with the human body or existing materials applied in a location not previously exposed to that material, and for which there is no convincing prior clinical experience, or where the device will be used for a significantly longer time.

4. Vigilance System

There are some Guidelines drafted through a process of intensive consultation of the various interested parties (Competent Authorities, Commission services of UE, industries, etc.) (3). They are legally not binding but they reflect positions taken by representatives of interested parties in the medical devices sector.

The purpose of the Vigilance System is to improve the protection of health and safety of patients, users and others by reducing the likelihood of the same type of adverse incident being repeated in different places at different times. This is to be achieved by the evaluation of reported incidents and, where appropriate, dissemination of information, which could be used to prevent such repetitions, or to alleviate the consequences of such incidents.

The Vigilance System is intended to allow data to be correlated between Competent Authorities and manufacturers and so facilitate corrective action earlier than would be the case if data were collected and action taken on a State by State basis.

Whilst the manufacturer has the responsibility for taking any action necessary, Competent Authorities should also monitor the effectiveness of the manufacturers’ follow-up on reported incidents. The Competent Authority should take any further action that may be necessary to supplement the actions of the manufacturer.

Once corrective (or other) action is identified, hospital administrators, medical practitioners and other health-care professionals, and user representatives responsible for the maintenance and the safety of medical devices can take the necessary steps. Such steps should, where practicable, be taken in co-operation with the manufacturer.

Competent Authorities may also monitor experience with devices of the same kind (for instance, all defibrillators or all syringes), but made by different manufacturers. They may then be able to take measures applicable to all devices of that kind. This could include, for example, initiating user education or suggesting re-classification.
Information held by Competent Authorities in connection with the Vigilance System is to be held in confidence, as defined by the relevant articles of the Directives. In order to achieve the purpose of the Vigilance System, any incident report should be available on request, and in confidence, to the other Competent Authorities.

The act of reporting an incident to a Competent Authority is not to be construed as an admission of liability for the incident and its consequences. Written reports may carry a disclaimer to this effect.

The initial report on an incident under the Vigilance System is made by the manufacturer to the Competent Authority for recording and evaluation. Each initial report should lead to a final report, but not every initial report will lead to a corrective action.

It is recommended that manufacturers inform their Notified Body of those incidents that may affect the certification provided by that Notified Body. However, it remains the role of the Competent Authority to monitor the investigation being carried out by the manufacturer.

Depending on the outcome of the investigation, any information necessary for the prevention of further incidents (or the limitation of their consequences) should be disseminated.

Therefore, in the Vigilance System are involved:
- manufacturers;
- competent authorities;
- notified bodies;
- health-care organisations and personnel (including the Scientific Associations).

4.1. Types of incidents to be reported

The types of incidents which a manufacturer should report to the Competent Authority are defined in the Directives as follows:
- Those which led to a death;
- Those which led to a serious deterioration in the state of health of a patient, user or other person. A serious deterioration in state of health can include:
  - life-threatening illness or injury;
  - permanent impairment of a body function or permanent damage to a body structure;
  - a condition necessitating medical or surgical intervention to prevent permanent impairment of a body function or permanent damage to a body structure.

The interpretation of the term ‘serious’ is not easy, and should be made in consultation with a medical practitioner wherever possible. Many points may need consideration, for example:
- whether a risk was foreseeable and clinically acceptable in view of potential patient benefit;
- whether the outcome was adversely affected by a pre-existing condition of the patient.

In cases of doubt on this issue, it is suggested that there should be a pre-disposition to report rather than not to report.
Not all incidents that should be reported involve a death or serious deterioration in health which actually occurred. The non-occurrence of such a result might have been due to other fortunate circumstances or to the intervention of health-care personnel. It is sufficient that:

– an incident associated with a device happened, and
– the incident was such that, if it occurred again, it might lead to death or serious deterioration in health, or
– an examination of the device or the information supplied with the device indicated some factor (e.g. a deterioration in characteristics or performance or a shortcoming in the information supplied) which could lead to an incident involving death or serious deterioration in health.

Such potential incidents are to be known as “near incidents”.

For a near incident to be reported, a possible direct link with the device, or with shortcomings in the information supplied, should be clearly established.

4.2. Time scaling for the initial reporting of an incident or near incident

The report should be made as soon as possible commensurate with determining whether the incident falls within the guidance discussed above. The times given below are the maximum elapsed times for determining the relevant facts and making the initial report.

The time runs from the manufacturer first being informed of the incident, to the relevant Competent Authority receiving the notification from the manufacturer:

– incidents 10 days
– near incidents 30 days

4.3. Vigilance System in Italy

As far as the post-market monitoring of MDs in Italy is concerned, the Competent Authority has defined certain obligations that manufacturers and health-care professionals must fulfil. The Legislative Decree of 24 February 1997, which transposes Directive 93/42/EEC in Italy, in its article 9 imposes health-care professionals, both public and private, the obligation to notify any incident involving a medical device of any class to the Ministry of Health.

Article 23 decrees that non-compliance with this obligation, unless it is regarded a penal indictable offence, is punished with a fine amounting from 5 to 30 million Italian Lira.

Article 10 decrees that the legal representatives of public or private health structures, and health-care professionals must immediately report the Ministry of Health on any alteration of the properties or performance of a medical device, or any inadequacy in the manufacturer’s instructions for use that led to the death or a serious deterioration in the state of health in the patient or user.

The same applies to manufacturers or their legal representatives, who also have to report the recall of a batch of devices from the market for technical or clinical reasons. Non-compliance with this obligation will entail confinement up to six months plus a fine amounting from 1 to 10 million Italian Lira.
Conclusion

As already stated, there are three critical aspects of the Directives:

– device classification;
– clinical investigation;
– post-market vigilance.

As for classification, we have seen there are four classes a device may be classified into. As the complexity of the relative certification process increases with class number, it is all too evident that manufacturers –if in doubt, or if classification rules are not clear enough– will tend to underrate the class their products belong in. On the contrary, the Competent Authority –under the same conditions– will tend to assign the product to a higher class for sake of public health protection. In such an eventuality the harmonisation is done by the European Commission by means of the Committee of Medical Devices.

As far as clinical investigation is concerned, Scientific Associations may help manufacturers elaborate ad hoc protocols to verify device efficacy and safety, and may collaborate with the Competent Authority in the evaluation of protocols and with the Notified Body in the evaluation of results.

Finally, in the sphere of post-market vigilance, the role of Scientific Associations could be, once again, that of trait d’union between Competent Authority and manufacturers, by evaluating manufacturers’ follow-up on reported incidents and, where appropriate, by disseminating information that can be used to prevent incident recurrence.

References

Directive 90/385/EEC (Active Implantable Medical Devices).
Directive 93/42/EEC (Medical Devices).
ENDOVASCULAR STENTS: SAFETY ISSUES

Mara Abbate, Carla Daniele, Giuseppe D’Avenio, Vincenzo Barbaro and Mauro Grigioni
Laboratorio di Ingegneria Biomedica, Istituto Superiore di Sanità, Roma

Introduction

In the last few decades, the world of interventional cardiology underwent a real revolution as a result of the introduction of endovascular coronary stents, small endoprostheses utilized to support the arterial wall and prevent its collapse. At first, these devices have been utilized as a support to traditional angioplasty to solve some problems linked to this procedure but, later on, thanks to the optimal results obtained, they have been used also “de novo” and gradually their use has been extended including patients categories previously excluded, and widening the range of indications for use. The success of stents, which went far beyond every possible forecast, was followed by the immediate response of manufacturers, which put on the market a great number of different brands and models, designed to satisfy the ever more diversified requirements of the operators.

Safety and reliability of the devices are monitored by means of the “post-market” surveillance, performed either by manufacturers or by scientific and governmental bodies. Surveillance is performed by collecting and analysing data coming from the greater possible number of reliable sources: board report analysis, institutes and/or university research, specialized reviews, consultation of database and, in general, every other means that supplies objective data about the medical device impact on the patient. These data, with those obtained from literature, provide a rich source of information about devices that can be used to recognize problems more frequently connected to coronary stents’ use and to prevent the occurrence of new ones. Moreover, data can be utilized in order to carry out the risk analysis of these devices, useful to improve the knowledge of the device and to try to limit risks connected to its use.

1. Data: collection and analysis

Currently a vast amount of clinical data is available, but these are obtained and produced using different and often not comparable methodologies. Data reported on single works regard nearly exclusively those of interest for the particular case in consideration, and they can be related with few other analogous cases. Details related to the procedural failures or to the accidents, that particularly interest those who take care of surveillance, are seldom reported. The situation improves a little as regards the trials in which data are often reported in a more detailed way. Unfortunately a standardized procedure of data collection doesn’t even exist in this case.

Among existing databases, FDA’s MAUDE (Manufacturer and User Facility Device Experience Database) contains reports about accidents related to all medical devices on the market in the United States. Reports are voluntary and regard problems connected to the use of devices (failures, inappropriate use, etc) that can have caused any kind of damage to the involved patients. Unfortunately this database does not contain information on a great number of stents available only on European markets.
1.1. FDA database

A study about coronary-stents-related accidents was carried out. Data analysis allowed to obtain information on coronary stents’ current safety level and to compare the different models available on the American market. A preliminary analysis has been carried out, classifying all reported accident related to the device and analysing the single hazard that determines a certain type of accident. Later on, the single stent models have been analysed and suitable comparisons have been made. The final classification of hazards related to coronary stents implantation is reported in Table 1. It can be noticed that most of the accidents are related to the first two hazard categories: stent came off from balloon and balloon malfunction. Results of the analysis clearly show that, in order to try to limit accidents, two main goals must be pursued: the first one is relative to the technical preparation of the medical staff who executes the implantation, the second regards device reliability that must guarantee an appropriate safety level, when utilized in conformity with instructions. Such safety level must be pursued in the design phase, in the materials’ choice, in the production cycles and, finally, in the test phase (carrying out, as an example, the check of compatibility with the accessories supplied with the stent or recommended as compatible with the latter).

Table 1. Hazard list

<table>
<thead>
<tr>
<th>Hazard</th>
<th>n.</th>
<th>Hazard</th>
<th>n.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent came off from balloon</td>
<td>819</td>
<td>Part of system/stent break-up</td>
<td>48</td>
</tr>
<tr>
<td>Balloon malfunction</td>
<td>413</td>
<td>System malfunction</td>
<td>40</td>
</tr>
<tr>
<td>Impossibility of stent deployment</td>
<td>36</td>
<td>Damaged/defective system</td>
<td>18</td>
</tr>
<tr>
<td>Wrong manoeuvre</td>
<td>46</td>
<td>Poor visibility</td>
<td>0</td>
</tr>
<tr>
<td>Not uniform/incomplete expansion</td>
<td>27</td>
<td>Loss of sterility</td>
<td>1</td>
</tr>
<tr>
<td>Complex or prolonged procedure</td>
<td>8</td>
<td>Allergy</td>
<td>2</td>
</tr>
<tr>
<td>Wrong choice of stent width</td>
<td>11</td>
<td>Wrong labelling</td>
<td>1</td>
</tr>
<tr>
<td>High susceptibility</td>
<td>1</td>
<td>Stent migration</td>
<td>18</td>
</tr>
<tr>
<td>Damaged/wrong packaging</td>
<td>3</td>
<td>Various</td>
<td>74</td>
</tr>
<tr>
<td>Structure break-up during expansion</td>
<td>3</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

As regards single stent analysis, various stent performances have been compared. In Table 2, as example, the percentage is showed of hazard occurrence for three stent models: Nir on Ranger, Crown and ACS.

Moreover stent procedure outcome, postprocedural complications and associated therapies have been analysed. Dissection and coronary perforation have been found to be the most common complications. Once again, therefore, it appears clear that a great experience in carrying out the catheter insertion and balloon inflation manoeuvres could drastically reduce such complications.

1.2. Literature data

As regards works reported on books and reviews, nearly all contain information about patients and diagnoses, followed procedures and data related to ospedalization and follow-up periods. Data related to the more interesting articles, such as trials, have been collected
in a database. Such data, associated to those related to the accidents, allow to consider a wider scenario, since they contain several additional information (like restenosis data, nearly completely absent from the FDA database). Articles, moreover, usually report more complete results, including either cases in which the procedure is successful or cases characterized by complications. This allows, as an example, to go back to the percentages of this complications, which aren’t deducible from accidents report.

Table 2. Percentage of hazard occurrence for Nir on Ranger, Crown and ACS Multilink

<table>
<thead>
<tr>
<th>Hazard</th>
<th>ACS multilink %</th>
<th>Crown %</th>
<th>Nir on Ranger %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent came off from balloon</td>
<td>46.7</td>
<td>41.2</td>
<td>22.4</td>
</tr>
<tr>
<td>Balloon malfunction</td>
<td>17.6</td>
<td>52.7</td>
<td>46.1</td>
</tr>
<tr>
<td>Part of system/stent break-up</td>
<td>9.3</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Wrong manoeuvre</td>
<td>7.7</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Various</td>
<td>4.8</td>
<td>1.8</td>
<td>23.7</td>
</tr>
<tr>
<td>System malfunction</td>
<td>2.7</td>
<td>2.2</td>
<td>2.6</td>
</tr>
<tr>
<td>Impossibility of stent deployment</td>
<td>2.7</td>
<td>1.3</td>
<td>1.3</td>
</tr>
<tr>
<td>Damaged/defective system</td>
<td>2.7</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Not uniform/incomplete expansion</td>
<td>2.1</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Wrong choice of stent width</td>
<td>1.1</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Complex or prolonged procedure</td>
<td>0.8</td>
<td>0.4</td>
<td>0.0</td>
</tr>
<tr>
<td>Stent migration</td>
<td>0.8</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Damaged/wrong packaging</td>
<td>0.5</td>
<td>0.0</td>
<td>0.0</td>
</tr>
<tr>
<td>Structure break-up during expansion</td>
<td>0.3</td>
<td>0.0</td>
<td>1.3</td>
</tr>
<tr>
<td>Loss of sterility</td>
<td>0.3</td>
<td>0.0</td>
<td>0.0</td>
</tr>
</tbody>
</table>

2. Risk analysis

The medical device risk analysis procedure, described on the European standard En 1441, includes three fundamental sections (analysis plan):

1. a complete description of the device and of its characteristics and a clear definition of the device and its possible accessories (functional analysis);
2. a list of all the potential hazard (preliminary hazards analysis);
3. a list of hazardous events (HE) associated to every possible identified hazard and the evaluation of the index of risk acceptability for every HE with the indication of the way in which this can be reduced to an acceptable level (classification of the HE or of the risks).

The acceptability risk index is estimated beginning from two components:

- the probability \( p \) that the hazard gives rise to an hazardous event that causes an harm;
- the gravity \( g \) of the harm related to the HE, defined by means of scales of values including a certain number of qualitative levels (probable, rare, etc.) associated to reference numerical values.

The probability \( p \) is given by the product of three probabilities:

1. probability \( p_1 \) that the possible hazard occurs (frequency, epidemiologic data);
2. probability \( p_2 \) that the HE occurs beginning from the identified hazard (literature data and accidents survey, e.g., FDA database);
3. probability \( p_3 \) that the HE involves an harm of gravity \( g \) (frequency, observable correlations).
According to the indications of the IEC 513 Technical Report, gravity of the harm has been defined by means of 4 levels, whereas probability of occurrence of each hazard has been defined by means of 7 levels. Risk acceptability index is determined by means of the criticality risk matrix (Table 3) given by the value at the intersection of the probability row and the gravity column ($p \times g$).

### Table 3 - Risk matrix

<table>
<thead>
<tr>
<th>Probability of Causing harm $P$</th>
<th>Harm gravity $G$</th>
<th>Catastrophic ($10^5$)</th>
<th>Critical ($10^4$)</th>
<th>Marginal ($10^3$)</th>
<th>Negligible ($10^0$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total $10^0$</td>
<td></td>
<td>$10^0$</td>
<td>$10^0$</td>
<td>$10^0$</td>
<td>$10^0$</td>
</tr>
<tr>
<td>Frequent $10^3$</td>
<td></td>
<td>$10^7$</td>
<td>$10^6$</td>
<td>$10^5$</td>
<td>$10^4$</td>
</tr>
<tr>
<td>Probable $10^4$</td>
<td></td>
<td>$10^7$</td>
<td>$10^6$</td>
<td>$10^5$</td>
<td>$10^4$</td>
</tr>
<tr>
<td>Occasional $10^5$</td>
<td></td>
<td>$10^8$</td>
<td>$10^7$</td>
<td>$10^6$</td>
<td>$10^5$</td>
</tr>
<tr>
<td>Remote $10^6$</td>
<td></td>
<td>$10^9$</td>
<td>$10^8$</td>
<td>$10^7$</td>
<td>$10^6$</td>
</tr>
<tr>
<td>Improbable $10^9$</td>
<td></td>
<td>$10^{10}$</td>
<td>$10^9$</td>
<td>$10^8$</td>
<td>$10^7$</td>
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<tr>
<td>Incredible $10^{10}$</td>
<td></td>
<td>$10^{11}$</td>
<td>$10^{10}$</td>
<td>$10^9$</td>
<td>$10^8$</td>
</tr>
</tbody>
</table>

Following the ALARP (As Low As Reasonable Practicable) risk philosophy, as in the EN 60601 normative, the matrix has been divided in four zones defined as follows:

- **Zone of intolerable risk** ($10^8-10^5$)
  - Risk is so high that it cannot be tolerated, a risk reduction is indispensable.

- **Zone of ALARP risk**
  - Risk must be reduced to the minimum possible level. The level in which the risk turns out “lower than it’s reasonably possible” is considered as minimal level.
    - Zone ALARP A ($10^4$): undesirable risk, tolerable only if its reduction is impracticable or the costs for the reduction are grossly disproportionated to the improvement gained.
    - Zone ALARP B ($10^3-10^2$): risk tolerable only if the costs of risk reduction would exceed the improvement gained.

- **Zone of roughly acceptable risk** ($10^1-10^{-1}$)
  - Risk negligible as regard the risk related to other hazards that are accepted. It is not necessary to actively search a solution to its reduction.

Risk analysis has shown that no hazard falls in the zone of risk “unacceptableness”. Instead, alarm zone (ALARP risk) interests some cases, i.e.:

- stent came off from the balloon;
- inadequate surface finishing (insufficient functional biocompatibility);
- wrong choice of stent width;
- not completely covered lesion;
- patient allergic to the contrast fluid;
- patient allergic to the utilized materials.

For these cases it is necessary to take appropriate measures to reduce the risk acceptability index.
Conclusions

As shown in the above discussion, surveillance is a rather complex operation, especially considering the fact that often nonhomogenous data are collected, according to different disciplinary criteria. Databases’ use is fundamental in this case, in view of integrating information deriving from different sources. It is essential, as well, to refine risk analysis, as the congruency of the collected data increases, with the aim of improving the evaluation of each device’s performance upon marketing approval. Then, the guidelines of the 93/42 Directive, concerning satisfaction of essential requirements, will be more safely applied.
**COMPUTATIONAL STUDY OF INTRAVASCULAR STENT MECHANICAL BEHAVIOR**

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(a) Dipartimento di Meccanica Strutturale, Università degli Studi di Pavia  
(b) Laboratorio di Meccanica delle Strutture Biologiche, Dipartimento di Bioingegneria, Politecnico di Milano

**Introduction**

Nowadays, the restoration of blood flow perfusion to the downstream tissues into stenotic arteries is commonly treated by the placement of expanded intravascular stents (1). They are small tube-like flexible structures, shaped as coil or strut, obtained by wires or tubes generally made of steel. The stent is mounted on a balloon catheter and delivered to the site of blockage. When the balloon is inflated, the stent expands and is pressed against the inner wall of the coronary artery. After the balloon is deflated and removed, the stent remains in place, keeping the artery open.

Different typologies of stents are available on the market and it is recognized the importance for the operator to know the different physical properties of the stent selected to treat a specific lesion. Moreover, clinical experience has showed a precise relation between stent geometry and its effectiveness. This observation suggests the necessity of a structural study to evaluate, to characterize and to optimize the stent behavior under different load (inflation pressure, bending, critical load) and to carry out fluid dynamic studies (2). Up to now, available useful information come from some experimental comparative studies (3): they give precise and accurate information, but they are also economically costing, as well as timely consuming.

Goal of the on-going research at the LABS (Laboratory of Biological Structure Mechanics) in collaboration with the Department of Structural Mechanics of the University of Pavia is to investigate the possibility of employing computational methods (4, 5), in particular Finite Elements Method, to integrate and eventually replace, in the initial phase of designing, *in vitro* experiments. With the commercial code ABAQUS (Hibbit Karlsson & Sorenses, Inc., Pawtucket, RI, USA) we realized:

- a 3D model (Figure 1) of a typical diamond-shaped coronary stent (Palmaz-Schatz\(^1\)) to understand the effects of different geometrical parameters (thickness, metal-to-artery surface ratio, longitudinal and circumferential\(^2\) cut lengths) on the device mechanical performance; Table 1 shows the geometric data of the reference model (DS) and of the 9 variant.
- two 3D models (Figure 2) of stents similar in the strut design to those nowadays available on the market, and comparable in terms of dimension (length, diameter, thickness of the strut) to the typical diamond-shaped stent model.

---

\(^1\) Johnson & Johnson, Interventional System, Warren, NJ, USA  
\(^2\) Defined by the ratio between \(\theta_s\), angle described by the metal surface and \(\theta_v\), angle described by the slot.
Materials and methods

The stent is assumed to be made of 316LN stainless steel. The inelastic constitutive response is described through a Von Mises-Hill plasticity model with isotropic hardening. Young modulus is 196 GPa, the Poisson ratio 0.3, the yield stress 205 MPa and the limit stress 515 MPa. The following analyses were performed:

- stent expansion by an internal linearly increasing uniform radial pressure (inflation) till the stent radius reaches, in the central region, the value of 1.5 mm, which is a reasonable value for an unobstructed coronary vessel; subsequent elastic recovery through pressure removal (deflation);
- stent expansion by an internal linearly increasing uniform radial pressure till the stent radius reaches, in the central region, the value of 2.0 mm.
The quantities calculated by the analyses and used to compare the different stent behavior were the ones commonly defined by the manufacturer claims. In particular, from the first type of simulations were calculated the following quantities:

- **the distal radial recoil**, defined as: \( \text{Distal Radial Recoil} = \frac{R_{\text{load distal}} - R_{\text{unload distal}}}{R_{\text{load distal}}} \)

- **the central radial recoil**, defined as: \( \text{Central Radial Recoil} = \frac{R_{\text{load central}} - R_{\text{unload central}}}{R_{\text{load central}}} \)

- **the longitudinal recoil**, defined as: \( \text{Longitudinal Recoil} = \frac{L_{\text{load}} - L_{\text{unload}}}{L_{\text{load}}} \)

- **the foreshortening**, defined as: \( \text{Foreshortening} = L - \frac{L_{\text{load}}}{L} \)

  where \( \text{load} \) means the maximum expansion position and \( \text{unload} \) means the zero pressure position; from the second type of simulations the following quantity was calculated:

- **the dogboning**, defined as: \( \text{Dogboning} = \frac{R_{\text{load distal}} - R_{\text{load central}}}{R_{\text{load distal}}} \)

  which is a measure of the different expansion between the central and the distal zone of the stent.

**Results**

**Diamond-shaped stent**

The results of the first type of analyses (Table 1) show the influence of the geometry on the stent behavior:

- increasing the ratio \( \alpha_p/\alpha_v \), the radial and longitudinal recoil decrease, while the foreshortening, the dogboning, the pressure necessary to reach a central radius of 1.5 mm \( (P_{1.5mm}) \) increase.
- decreasing the thickness \( s \), the longitudinal recoil, the foreshortening, the dogboning increase, while the pressure \( P_{1.5mm} \) decreases. The radial recoil does not seem to be significantly influenced by the thickness variation.
- increasing the slot length \( L \), the radial and longitudinal recoil increase, while the other quantities are not significantly influenced by its variation.

The second series of simulations evinced the strong influence of the metal/artery ratio \( (\alpha_p/\alpha_v) \) on the pressure increment necessary to expand the stent up to a radius of 2 mm in the central zone as well as on the dogboning (Figure 3). Being this effect undesirable, the results suggested to consider a new model \( (DS_{mod}) \) modifying the model \( DS \): the dimension of the 12 circumferential slots in the distal part were reduced, increasing the \( \alpha_p/\alpha_v \) ratio from 0.3 to 0.6.

15
Table 1. Geometric data and results

<table>
<thead>
<tr>
<th>Model</th>
<th>Geometric parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>s (mm)</td>
<td>L (mm)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DS</td>
<td>0.1</td>
<td>2.88</td>
</tr>
<tr>
<td>DS1</td>
<td>0.1</td>
<td>2.88</td>
</tr>
<tr>
<td>DS2</td>
<td>0.1</td>
<td>2.88</td>
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</tr>
<tr>
<td>DS4</td>
<td>0.1</td>
<td>2.96</td>
</tr>
</tbody>
</table>

s: thickness; L: cut length; m/a: metal-to-artery ratio; C: central; D: distal.

Figure 3. Comparison between distal and central radius expansion for diamond-shaped models.
Dot line represents the uniform stent expansion.
Stents with different geometry

Figure 4 shows the effect of different geometries on the central and radial expansion.

In the modified distal geometry ($DS_{mod}$), the distal nodes have smaller radial displacement than the central ones (dogboning - 46.25%); varying the ratio $\alpha_p/\alpha_v$, it is possible to control the dogboning effect, up to obtain an opposite effect. In the model $GEO1$ the distal expansion has a different behavior according to the orientation of the ring pattern: in the ‘distal zone 1’ (Figure 2) the expansion is more pronounced than in the ‘distal zone 2’, where an effect opposite to the dogboning is present (Table 2). This peculiar behavior is due to the particular stent design and the loading type applied. In the model $GEO2$ the central and distal radial expansion are similar and the dogboning effect is nearly absent. Finally, model $DS_{mod}$ and $GEO2$ have a radial recoil comparable with model $DS$, while model $GEO1$ does not show any recoil; the foreshortening in the model $DS_{mod}$ is lower than in model $DS$, while models $GEO1$ and $GEO2$ show higher values.

Table 2. Results for the two different types of stent geometry

<table>
<thead>
<tr>
<th>Model</th>
<th>Geometric parameters</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zone</td>
<td>s (mm)</td>
<td>m/a</td>
</tr>
<tr>
<td>GEO1</td>
<td>0.1</td>
<td>0.341</td>
</tr>
<tr>
<td>GEO2</td>
<td>0.1</td>
<td>0.345</td>
</tr>
</tbody>
</table>

$s$: thickness; m/a: metal-to-artery ratio.

Figure 4. Comparison between distal and central radius expansion for models $DS$, $DS_{mod}$, $GEO1$ and $GEO2$. Dot line as in Figure 3.
Conclusions

Although the lack of the interaction artery-stent in our models is a strong limitation that we are trying to overcome, these results are promising and useful in the study of stent mechanical performances: a finite element analysis similar to the one herewith proposed could help in designing new stents or analysing actual stents to ensure ideal expansion and structural integrity, substituting and/or supporting in vitro experiments often difficult and unpractical.

References

GALERKIN METHOD FOR FLUIDS IN DOMAINS WITH ELASTIC WALLS

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Dipartimento di Matematica, Università di Ferrara

To solve the problem of simulation of blood in arteries, in Quarteroni et al. and Formaggia et al., the so-called generalized string model is proposed. In Beirao Da Veiga it is proven an existence theorem of strong, local in time, solutions with small initial data. Here we propose a different method to prove existence of weak, global in time, solutions with small data. The method is the so called Galerkin approximation, and requires the knowledge of a basis in a Hilbert space, say \( L^2(\Omega) \), where \( \Omega \) is the domain filled by the fluid. In this case the domain is function of time, and this creates the major difficulty.

1. Position of the problem

Let \( R = [0, i, j, k] \) be a orthonormal reference frame, and denote by \((x, y, z)\) the coordinates of a point in the space. In the plane \( z = 0 \) we consider the two-dimensional domain of area \( \Omega, = \{(x, y) \in R^2 : \ x \in (0,1), 0 < y < 1 + \eta(x, t)\} \) with \( \int_0^1 \eta(x, t) dx = 0 \), furthermore, on the boundary \( \Gamma = \{(x, y) \in R^2 : \ x \in (0,1), \ y = 1 + \eta(x, t)\} \), we denote by \( n \) the normal to \( \Gamma \). We set \( g = 1 + \left( \frac{\partial \eta}{\partial x} \right)^2 \), and remind that \( n = (n_x, n_y, 0) = \left(-\frac{\partial \eta}{\partial x}, 1, 0\right) \). The model proposed in [6], [7] is described by the following initial boundary value problem

\[
\nabla \cdot \mathbf{v} = 0, \quad \frac{\partial \mathbf{v}}{\partial t} + \mathbf{v} \cdot \nabla \mathbf{v} = \nu \nabla S(\mathbf{v}) - \nabla p, \quad x, y \in \Omega, \\
\frac{\partial^2 \eta}{\partial t^2} = \beta \frac{\partial^2 \eta}{\partial x^2} - \gamma \frac{\partial^2 \eta}{\partial t \partial x} + \alpha \frac{\partial \eta}{\partial x} + \sigma \eta = H(\eta), \quad x \in (0, 1); \\
H(\eta) = p - \nu n \cdot \nabla \eta, \quad t \cdot \nabla \eta = 0 \quad \text{on } \Gamma; \\
\mathbf{v} \cdot n = \frac{\partial \eta}{\partial t} n_y, \quad x, y \in \Gamma; \\
\mathbf{v}(x, 0, t) = 0, \quad x \in (0, 1); \\
\mathbf{v}(x, y, 0) = \mathbf{v}_0(x, y), \quad x, y \in \Omega_0, \quad \eta(x, 0) = \eta_0(x), \quad \eta_t(x, 0) = \eta_1(x), \quad x \in (0, 1).
\]

(1.1)

The constants \( \alpha, \beta, \gamma, \sigma \) characteristic of the elastic boundary are positive constants, \( \nu \) is the kinematical viscosity, furthermore, \( S(\mathbf{v}) \) denotes the symmetric part of the velocity gradient tensor \( S(\mathbf{v}) = \nabla \mathbf{v} + (\nabla \mathbf{v})^T \).
On the part of the boundary \( x = 0, x = 1 \) we assume periodicity, precisely, for \( \eta \in H^1(\Omega) \) with zero value at \( y = 0 \) and periodic in \( x \), we write \( u \in H^1_h(\Omega) \), for \( \eta \in H^2(0,1) \), periodic in \( x \) we write \( \eta \in H^2(0,1) \).

We prove the following existence theorem

**Theorem 1** Let \( v_0 \in L^2(\Omega), \eta_0 \in H^2(0,1), \eta_1 \in L^2(0,1) \), satisfying the compatibility condition

\[
v_0 \cdot n(x, \eta(x,0),0) = \eta_1(x)n_1(x,0)
\]

and let

\[
\int_{\Omega} v_0^2 dx dy + \int_0^1 \eta_1^2 dx + \beta \int_0^1 \eta^2_0 dx + \alpha \int_0^1 \eta_0^2 dx + \sigma \int_0^1 \eta^2 dx < \frac{1}{4}.
\]

(1.2)

Then, there exists a global solution to (1.1) with \( v \in L^\infty(0,T;L^2(\Omega)), \eta \in L^\infty(0,T;H^1(\Omega)), \eta \in L^2(0,T;H^2(0,1)), \eta \in L^2(0,T;H^1(0,1)) \cap L^\infty(0,T;L^2(0,1)) \).

2. Existence proof

We prove that problem (1.1) has a solution. We use a modification of Galerkin procedure, since the domain is unknown and we are lead to choose suitably the basis, this problem has still open problems. To this end, in two dimensions we consider the stream function \( \psi = \nabla \times k \), with \( k \) direction orthogonal to the plane \( x, y \), so that we are reduced to exhibit a scalar basis in \( H^2(\Omega) \). Thus, we look for a decomposition in product of two functions, one of \( x \) only, \( \alpha_k(x) \), and one of \( y \) only, \( \beta_k(y) \). For \( \alpha_k(x) \) we choose sinusoidal functions that satisfy periodicity at \( x = 0, x = 1 \). For \( \beta_k(y) \) we choose polinomial functions \( y^n \). Summarizing, we look for a vector basis \( \mathbf{a}_k(x, y) \) in \( H^1_h(\Omega) \) in the form

\[
\mathbf{a}_k(x, y) = \nabla \psi_k(x, y) \times k, \quad \psi_k(x, y) = \alpha_k(x)\beta_k(y).
\]

The orthogonality condition \( \int_\Omega \alpha \alpha_k dx = \delta_{kl} \) is obviously satisfied. Furthermore, by changing the variable \( y = (1 + \eta) \), we have

\[
F_{ik}^n(l) = \int_0^1 \int_l^{1+n\eta(x)l} \beta_i(y)\alpha_j(x) \cdot \alpha_k(x) dy dx = \int_0^1 1 + \eta^n(x, l)^{l+1} \frac{\alpha_j(x)\alpha_k(x) dx}{l+1},
\]

that, for \( \eta^n < 1/4 \), and \( l \) fixed is an invertible matrix.

By \( H^1(\eta^n) \) we mean (1.1), and set \( \Gamma_{i}^n = \{ x, y \in R^2 : x \in (0,1), y = 1 + \eta^n(x, l) \} \), and
We look for a solution \( \mathbf{v}^n \) in the form

\[
\mathbf{v}^n = \sum_{i,j=1}^n c^a_{ij}(x) \mathbf{a}_i \mathbf{a}_j(x).
\]

Inspired by Galerkin procedure, we look for an approximating solution \( \mathbf{v}^n \) of the mixed ordinary, partial system

\[
\begin{align*}
\sum_{j=1}^n \frac{d c^a_{ij}}{dt}(a_{ij}, a_{ik})_{t}^n + \sum_{s,r=1}^n c^a_{ij} c^a_{rs}(a_{rs} \cdot \nabla a_{ij}, a_{ik})_{t}^n &= \\
= -\nu \sum_{j=1}^n c^a_{ij} \left(S(a_{ij}), S(a_{ik})\right)_{t}^n - \int_{\Gamma^n} H(\eta^n)n_{ik} \cdot j dS_n,
\end{align*}
\]

(2.1)

where \( \mathbf{j} \) denotes the direction of the \( y \) axis, \((a_{ij}), (a_{ij})_y\) are the components of \( a_{ij} \) onto the axes \( x, y \) respectively. Notice that, summing over \( i \) we deduce

\[
\begin{align*}
\left( \frac{\partial \mathbf{v}^n}{\partial t}, a_{ik} \right)_{t}^n + \left( \mathbf{v}^n \cdot \nabla \mathbf{v}^n, a_{ik} \right)_{t}^n &= \\
= -\nu \left(S(\mathbf{v}^n), S(a_{ik})\right)_{t}^n - \int_{\Gamma^n} H(\eta^n)n_{ik} \cdot j dS_n, \quad k = 1, \ldots, n
\end{align*}
\]

(2.2)

where \( \mathbf{v}_x, \mathbf{v}_y \) are the components of \( \mathbf{v} \) along \( i, j \). To avoid heavy notations, we have used the symbol \( n \) also to denote the normal to the approximating free surface \( \Gamma^n \),

\[
\mathbf{n} = [n_x, n_y, 0] = \left( -\frac{\partial \eta^n}{\partial x}, 1 \right) \left( g^n \right)^{1/2}.
\]

Therefore, (2.1) is a more refined equation than (2.2).

To (2.1), we append the initial conditions

\[
\mathbf{v}^n(x,y,0) = \mathbf{v}_0^0(x,y), \quad \eta^n(x,0) = \eta_0^0(x), \quad \eta_t^n(x,0) = \eta_t^0(x).
\]

(2.3)
Consistency of the scheme

Provided the solution $v^n$, $\eta^n$ exists and is convergent to $v$, $\eta$, there exists a function $p$ such that the stress tensor $vS - pI$ satisfies at the boundary $\Gamma$,

$$H(\eta) = p - v_n \cdot S_n, \quad t \cdot S_n = 0, \text{ on } \Gamma_t,$$

therefore, we recover system (1.1).

Construction of the approximating solution

Let us consider the trajectory $\chi^n(x_0, y_0, t)$ that solves

$$\frac{d\chi^n}{dt} = v^n(\chi^n, t), \quad \chi^n(x_0, y_0, 0) = (x_0, y_0).$$

(2.5)

For $\eta^n$ we can consider the explicit solution, in terms of $v^n$, along the trajectory

$$\eta^n(\chi^n(x_0, y_0, t), t) = \eta^n_0(x_0, y_0) + \int_0^t v^n(\chi^n(x_0, y_0, s), s) ds.$$

(2.6)

To prove that (2.1) can be put in normal form in terms of $c^{nk}(t)$, we must prove the invertibility of $F^{nk}$, that is proven once $\eta^n < 1/4$ is proven. To this end, first we derive the energy estimate from (2.2). Indeed multiplying (2.2) by $c^{nk}(t)$ and summing over $i, k, l$ we deduce, for $i, k, l = 1, \ldots, n$

$$\left(\frac{dv^n}{dt}, v^n\right)_t + \left(v^n \cdot \nabla v^n, v^n\right)_t =$$

$$= -\nu (S(v^n), S(v^n))_t - \int_{\Gamma_t} H(\eta^n) v^n \cdot \nu dS_n.$$

(2.7)

by careful use of the transport theorem, using the boundary conditions $v^n \cdot n = n \frac{\partial \eta^n}{\partial t}$, and employing the definition of $H$ at the right hand side of (2.7), since $(0; 1)$ is a fixed interval, we obtain the energy estimate
Integrating (2.8) in time we deduce

\[
\int_{\Omega_t} (v^n)^2 dxdy + \int_0^1 \left\{ \left( \frac{\partial \eta^n}{\partial t} \right)^2 + \alpha \left( \frac{\partial^2 \eta^n}{\partial x^2} \right)^2 \right\} dx + \int_0^t \int_{\Omega_t} S^2(v^n) dxdyds \leq
\]

\[
\gamma \int_0^t \int_{\Omega_t} \left( \frac{\partial^2 \eta^n}{\partial x^2} \right)^2 dxdy + \int_0^t \{ \eta^n \}^2 dx + \alpha \left( \frac{\partial^2 \eta^n}{\partial x^2} \right)^2 + \beta \left( \frac{\partial \eta^n}{\partial x} \right)^2 \right\} dx.
\]

(2.9)

In particular from initial condition on the data (1.2) we claim that \(\sup_{x \in (0,1)} \eta^n(x,t) < 1/4\) for all time instant \(t\). This result is crucial in the proof of existence of \( n^{n+1} \), as we shall see below.

**Existence of \( n^{n+1} \) and \( \eta^n \)**

We have proved that the matrix \( F^n_{jk} \) is invertible. Thus solving the algebraic system (2.2), in the unknown \( \frac{dc^n_{jk}}{dt} \), we rewrite system (2.2) in the form

\[
\frac{dc^n_{ij}}{dt} + \sum_{r,s,j,k=1}^n A^n_{ij,l,k,l,r,s}(t)c^n_{ij}c^n_{rs} =
\]

\[
= -\nu \sum_{i=1}^n c^0_{ij} B^n_{ij,l,l,k}(t) - \sum_{j=1}^n C^n_{jk}(t) \int_{\Gamma_+} H(\eta^n) u_{ik} \cdot J \partial S_n,
\]

(2.10)

with obvious meaning for the coefficients \( A^n_{ij,l,k,r,s}(t) \), \( B^n_{ij,l,k}(t) \), \( C^n_{jk}(t) \). System (2.10) is in normal form in the unknowns \( c^0_{ij} \) and \( \eta^n \). By Cauchy-Kowaleskaja theorem, for fixed \( n \), we know that there exists a time \( \tilde{t} \) such that there exists only one solution to (2.10). The solution is also global since, again from energy inequality (2.9), we deduce that
with a suitable positive constant. The boundedness of the approximate solution for all times, allows us to state that there exists a global regular solution to (2.2) uniformly bounded in the space

Thus we claim that there exists a weak limit \( v, \eta \) for the given sequence.

**Uniform continuity of the approximating sequence**

The uniform continuity in time follows from (2.13) integrated from \( t \) to \( t + \Delta t \), noticing that \( \eta^n \) has time derivatives uniformly bounded. The proof follows standard methods [5], with non trivial calculations.

**Convergence of the approximating sequence**

By weak compactness theorems it follows the existence of a subsequence that we continue to denote by \( v^n, \eta^n \) and a limit \( v, \eta \), which is defined for all time \( t \) and belongs to the same spaces of the approximating sequence, such that

1. \( S(v^n) \) converges weakly to \( S(v) \) in \( L^2([0,T];L^2(\Omega)) \);
2. \( v^n \) converges weak-star to \( v \) in \( L^\infty([0,T];L^2(\Omega)) \);
3. \( \eta^n \) converges weak-star to \( \eta \) in \( L^\infty([0,T];L^2(\Omega)) \);
4. \( \eta_{xx}^n \) converges weak-star to \( \eta_{xx} \) in \( L^\infty([0,T];L^2(\Omega)) \);
5. \( \eta_{tt}^n \) converges weakly to \( \eta_{tt} \) in \( L^\infty([0,T];L^2(\Omega)) \).

From these convergences we deduce also the strong convergence of our sequences in larger spaces, and this together with the equicontinuity allows us to claim that the limit is still solution of (2.2) for any fixed \( k \). Multiplying (2.2) by a function \( \psi_k(t) \) and summing over \( k \) we obtain a function \( \Psi_k \) in the finite dimensional space. Passing to the limit \( n \to \infty \) we
first obtain the limit solution in a finite dimensional space. Thus letting \( \Psi \) be varying with \( k \in \mathbb{N} \), \( \mathbb{N} \) natural numbers, we find the wanted equation of the motion.

**Acknowledgements**

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VELOCITY FIELDS AND PROPAGATION PHENOMENA
IN THE ARTERIAL SYSTEM

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**Introduction**

A lot of studies have been devoted to investigate the arterial system and it is impossible
to report, in a limited space, even a synthetic description. Ku (1997) provides a recent and
excellent bibliographic review. It is known from literature that, for a satisfactory descrip-
tion of the system, it is too onerous and not strictly necessary to use three-dimensional
models for the study of propagation phenomena. However, it is important to take into ac-
count at least the variability of the velocity profiles along the radius, because they are dif-
ferent than the parabolic profiles considered in one-dimensional models, which are valid
only for uniform flow.

Following these considerations, the development of a two-dimensional model of the ar-
terial system (Pezzinga, 1997) is presented, investigating the effect of the radial convection
terms, previously neglected.

**1. Mathematical model**

The human arterial system is illustrated in Figure 1. The elements of the system are the
arteries, considered as vessels having elastic behaviour. Some of them deliver a distributed
outflow. In the distal sections of the terminal vessels and in some internal junctions, a con-
centrated outflow is considered.

Under previously discussed hypotheses (Pezzinga, 1997), the equation of axial-symmet-
ric flow may be written in cylindrical coordinates in the form:

\[
\frac{\partial A}{\partial t} + \frac{\partial Q}{\partial x} + q_e = 0
\]  

\[
\frac{\partial U}{\partial t} + U \frac{\partial U}{\partial x} + V \frac{\partial U}{\partial r} = - \frac{1}{\rho} \frac{\partial p}{\partial x} + g \sin \alpha - \frac{1}{\rho r} \frac{\partial (r \tau)}{\partial r}
\]  

where \(A\) is the cross-sectional area, \(Q\) is the discharge, \(q_e\) is the outflow per unit length, \(t\) is
the time, \(x\) is the abscissa, \(r\) is the distance from the axis, \(U\) and \(V\) are the velocity
components respectively in the \(x\) and \(r\) directions, \(\rho\) is the density, \(p\) is the pressure, \(g\) is the
gravitational acceleration, \(\alpha\) is the angle with respect to the horizontal direction and \(\tau\) is the
shear stress.

The radial velocity component \(V\) relative to the generic cylindrical moving surface with
radius \(r\) can be obtained by the continuity equation:

\[
\frac{\partial}{\partial t} \int_{0}^{r} 2\pi r \eta d\eta + \frac{\partial}{\partial x} \int_{0}^{r} U 2\pi r \eta d\eta + 2\pi r V = 0
\]
The dependent variables are area and velocity: all the other variables are obtained afterwards by algebraic relations or by integration. In particular, pressure is obtained from the area through the relationship:

\[ p = p_e + \rho c_0^2 \left( 1 - \frac{A_0}{A} \right) \]  

where \( p_e \) is the external pressure (assumed constant) and \( A_0 \) and \( c_0 \) are the values of area and wave speed for \( p = p_e = 0 \). The diameter \( D_0 \) and the wave speed \( c_0 \) are considered to vary linearly from the proximal to the distal ends of the vessel. The distributed outflow is related, through empirical coefficients, to the difference between internal and external pressure, by a power law.

In order to perform the integration of the equations, some boundary conditions must be defined.

In particular, the inlet flow at the proximal end of the ascending aorta is assumed to vary as reported, for a period \( T_p \), in Figure 2.

At the distal ends of terminal vessels, furthermore, a concentrated outflow is considered, described by a power law similar to the one considered for distributed outflow.

At the internal junctions, finally, uniqueness of the pressure and continuity of the flows are imposed. The continuity equation is written for the volume of the final half meshes of vessels joining at the junction (Figure 3); once the volume is known, it is possible to determine the pressure at the junction (Pezzinga, 1997).

At some junctions there is an outflow described by a relation similar to the one considered for terminal junctions.
Besides the two-dimensional model just described, both a one-dimensional model similar to the one proposed by Noseda (1974), and a two-dimensional model in which the radial velocity component in the momentum equation is neglected (Pezzinga, 1997), are considered. It is possible to refer to the work of Noseda also for all the theoretical hypotheses, independent of the one-dimensional or two-dimensional schematisation of the flow.

2. Numerical scheme

The integration of the previously described equations is made by the McCormack scheme, second order explicit, adapted to a cylindrical grid with staggered meshes moving in the radial direction. The meshes have the same cross-sectional area, varying in time. The scheme is defined by two subsequent steps: the predictor step, in which the discretization of flux terms and source terms is referred to the previous time step values, and the corrector step, in which the predictor step values are considered. Due to the staggered grid, only for the convection terms the evaluation of the derivatives in the \( \Delta x \) direction are computed alternatively forward and backward in the predictor step and in the corrector step. The final value of each dependent variable (area and velocity) is calculated as the average of the predictor step and of the corrector step values. All the terms are evaluated explicitly, except for the radial convection term and the resistance term in the momentum equation, which need an implicit formulation. For the solution of the relevant convection-diffusion problem, a hybrid scheme is adopted. Also the boundary conditions providing the pressure values at the distal ends of terminal vessels are discretized by a predictor-corrector scheme.

The momentum equation in the simplified two-dimensional model is solved in a similar way but, as the radial convection term is neglected, the problem is simply diffusive, and then a centred scheme is used. In the one-dimensional model all terms are evaluated explicitly.

3. Analysis of results

Some cases were considered among those studied by Noseda, looking at the results in the same control sections. The values of the physical parameters used in the computations can be found in the mentioned work; with regard to the numerical parameters, each vessel is subdivided into as many longitudinal meshes as those used by Noseda and in 50 radial
meshes of equal area (varying in time). In the following figures, for sake of brevity, only the results obtained in the simpler case (case A) are reported, that is for a man in horizontal position and in normal physiological conditions. In particular, Figure 4 shows the pressure in the initial section of the ascending aorta (Sect. 1) and in the final section of the posterior tibial artery (Sect. 22), compared with the pressure computed by the one-dimensional model. A pressure oscillations damping due to the evaluation of resistances from velocity profiles is evident in the peripheral section.

A comparison between computed pressure by both two-dimensional models shows that the results are practically equal.

On the contrary, the comparison between longitudinal velocity profiles (Figure 5) shows that, near the heart, to take into account the radial velocity component considerably influences the results: indeed such component, although two order of magnitude smaller than the longitudinal one (Figure 6), makes more uniform the longitudinal velocity component profiles. Instead, in peripheral regions the contribution of the radial convection terms is slight, and the profiles computed by both models tend to be very similar and to have behaviour close to the parabolic law.
Conclusions

The investigation regards the development of a two-dimensional model of the arterial system previously presented, with the aim of examining the effect of the radial convection terms on the results. In particular, when such terms are taken into consideration, the velocity profiles are appreciably modified only near the heart and less and less towards the peripheral regions. On the other hand, the computed pressures are very similar.

The model in its present form seems to be general enough to examine the effect of distributed resistances on propagation phenomena in the arterial system. However further studies are planned to extend the model in order to consider the effect of local variations of geometry and of elastic properties of vessels.

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References

NUMERICAL STUDY OF BLOOD DYNAMICS IN VASCULAR ACCESS METHODS: VENOUS CANNULATION

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Vascular access methods, performed by the insertion of cannulae into vessels, may disturb the blood flow giving rise to non physiological behaviour, whose consequences can result in a decreased longevity, in a change to the membrane properties or, as a worst case, in a complete destruction of blood cells. Till now, the hydrodynamical behaviour of the cannulae has been evaluated comparing their in vitro obtained relationships between pressure drop and flow rate, that do not furnish any information about the local fluid dynamics established into the vessel and the inserted cannula in clinical conditions. As a consequence, speculations on the possibility to predict blood sublytic or lytic trauma, or blood interaction with external surfaces, suffer from the lack of data. Even design improvement procedures and a major control in surgical practices, addressed to bound blood shearing, are poorly supported by detailed knowledge of the involved phenomena. A powerful instrument to study the fluid dynamics as accurately as possible, starting from a simulated flow field, is given by numeric studies. We chose a simple device, a venous cannula, to investigate the relevance of both design features and its appropriate use: a parametric 3D realistic model simulating blood dynamics in a cannula concentrically placed in a rigid wall vessel has been realized, with the FEM used to numerically simulate the steady state flow field in two different venous cannulation case studies, with cannulae having a central hole and 2 and 4 side holes respectively, and the same boundary conditions. Blood was modelled as an homogeneous, incompressible Newtonian fluid, flow was assumed to be laminar.

The effect on blood dynamics of the different number of side holes reveals itself with a maximum value for the shear rate the 40% higher for the model with 2 side holes than for the model with 4 ones. For the cannula with 4 side holes the morphology of the velocity profiles was found to be more regular, thanks to the higher symmetry, with respect to the model with 2 side holes. As a consequence of both a larger inlet area and a higher level of symmetry, lower peak values of both the axial velocity and the shear rate have been computed, together with a lower pressure loss for the blood motion through the cannula (a pressure drop the 40% higher for the model with two side holes). Number and position of side holes play a relevant role also in the distribution of blood suction: the cannula with 4 side holes distributes the inlet blood flow almost in equal manner between all the holes while, for the model with 2 side holes, blood flows for the 38.25% from each lateral hole (with the side hole area 17.28% greater than the central one).

The computed data allow us to observe that, in working conditions corresponding to not complete venous blood drainage, the interaction between the vessel and the inserted cannula could be taken into account: in fact, the presence of blood flow between cannula
and vessel may be responsible for the onset of shear rate values inducing not physiological reactions onto the external walls of the cannula and of the vessel. For the two models, under the imposed boundary conditions, we computed the highest values of shear rate outside the cannula in its cylindrical tract, being the WSR between vessel and cannula mainly a consequence of the free luminal space left by the inserted cannula.

The presence and the symmetrical location of a higher number of holes in the cannula reduced the shear rate values (1700 s\(^{-1}\) and 1380 s\(^{-1}\) the values computed for the cannulae with 2 and 4 side holes respectively), particularly in the cannula’s tip region: under the hypothesis of accumulation of damage on sheared blood particles, leading to a gradual deterioration of the cellular blood elements, it must be taken into account that also apparently low levels of shear stress (SS) can result in potential clinical problems (during circulatory supports, blood travels through the cannula several times; furthermore, blood flows also through other potentially traumatic devices). Therefore it is necessary to reduce as much as possible the mechanical load on blood constituents.

Shear rate values higher than the physiological ones imply emphasized cellular sublytic phenomena, with significant consequences on platelets aggregation process. Sublethal red blood cells damage due to membrane deformation, occurs at stresses well below that needed for actual red blood cells lysis (1). The intracellular compound ADP is released from red blood cells damaged by SS, triggering subsequent platelet aggregation. Microaggregates, suspected to cause microvascular occlusion and tissue morbidity in extracorporeal flow can be partially attributed to platelet activation caused by the exposition to SS during extracorporeal flow. Shearing blood \textit{in vitro} with SSs in the order of 10 Pa, the release of ADP from platelets has been shown to result in minute concentrations: Hall \textit{et al.} reported the formation of rigid platelets microaggregates in response to low concentrations of ADP in whole heparinized blood. Because these ADP concentrations are similar to those released by platelets or red blood cells when exposed to SSs found in extracorporeal circuits, ADP induced aggregation may be important during extracorporeal circulation (2).

We found SS peak values of 6.15 and 4.97 Pa for the models with 2 and 4 side holes respectively: as even in sublethal conditions a release of ADP may occur (2), the computed shear SSs are not so low to exclude an ADP release sufficient for triggering platelet aggregation, so that it is important to reduce shearing as much as possible. The cannula with 4 side holes, exhibiting SS values lower than the other model, reduces the possibility of sublethal damage and ADP release, with a consequent reduction of the probability of microaggregate formation. The presented results have, thus, a possible clinical implication, because the hemodynamics of the considered devices can elicit aggregative phenomena. The occlusive microaggregates eventually produced by low concentrations of ADP during extracorporeal circulation may be trapped in the microvasculature or in hollow fibers or filters. Such trapping may be related to platelet loss and consequently may contribute to tissue morbidity and neurologic dysfunction.

The computed 3D blood flow pattern have been used to describe particle pathlines (3). The Lagrangian ‘visualization’ technique has made us easier the comprehension of the flow rate distribution entering the cannula and the effect of side holes on it. Figure 1 shows some particle trajectories entering the vessel’s inlet, relatives to both the two case studies: as far as the model with 2 side holes, the computed tracks visualized in Figure1a highlight how blood entering the central hole arises largely from the high speed core around the vessel’s
centerline (e.g., $z$ axis direction); in contrast, flow outgoing from the cannula around the vessel’s centerline is fed largely by the slower, peripheral flow at the inlet of the vessel (Figure 1b).

Furthermore, the level of uniformity of the blood flow seems to be related with the onset of pronounced helicoidal motion of the particles.

The association between specific non physiological flow patterns and blood particles shearing suggests that a 3D perspective visualization of the paths may be used, color-coding the pathlines in a variety of ways, with the aim to provide the observer of an easy instrument to investigate hemodynamic features potentially leading to risks of blood denaturation, as well as to evaluate flow dynamics in cardiovascular interventions.

References

A COMPUTATIONAL MODEL OF FLOW IN STENTED ELASTIC ARTERY

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Unsteady flow in conduits with elastic walls is of special interest for the cardiovascular systems in order to understand the phenomena involved, predict the evolution of pathologies due to vessel deformation and the hydraulic behaviour after the insertion of a prosthesis.

An alteration of the arterial wall is characterised by an accumulation of lipidic material and a progressive thickening of vascular walls. This process eventually causes stenosis, a narrowing of the vascular lumen whose entity represents a determining factor for the ictus risk.

The normal surgical treatment for arterial pathologies consists of a cut on the vessel neck to remove the nidificated fat that reduces the blood flow lumen. The endovascular technique is another less invasive option, it consists of a prosthesis insertion, a stent.

It is possible to find either publications of experimental studies results (1, 2) regarding the arterial wall answer to the endovascular prosthesis and other studies on the biomechanics interaction between a stent and a stenotic artery proposing a modified stents typology (3-5) in order to limit the restenosis process. There are also studies estimating the wall shear stress distribution in a stented artery such as a factor connected to the cellular and thrombi increase (6).

We study a pulsatile flow inside a circular vessel with variable section and elasticity, as a model for a stented elastic artery under ideal conditions. The objective is to verify the main flow modifications that are present in an elastic circular vessel in presence of a compliance mismatch which is also assumed to occur in correspondence of a slight vessel enlargement.

The analysis is performed by computational techniques. The modelling of flow over elastic boundaries deserves several difficulties because the fluid and the wall are coupled in a strong interaction. Thus the unsteady solution is hardly found by iteratively solving the flow and tissue equations rather a coupled solution technique is commonly required.

We introduce a perturbative approach for the solution of pulsatile flow inside moderately elastic arteries (7). It is an approximate method that appears to be appropriate for the study of spatially limited district in large artery flow because of the following facts. The pulsation period is very large when compared with the convective time scale (e.g. the Strouhal number is small, order 10-2), propagation phenomena have such a long wavelength, say not less that some ten diameter, that can be assumed as synchronous when making local analysis. The pressure variation along the vessel are negligible when compared to the physiologic (systolic-diastolic) pressure changes in time, therefore, locally, deformations are mainly driven by the external forcing (boundary conditions) and not by the flow itself. Finally, the artery stiffness is often large enough that wall deformation is of relatively small entity, well below 10% of the vessel diameter, and a small perturbation approximation can be employed.
A preliminary evaluation of the flow alteration in a stented rectilinear vessel is done using a complete coupled solution under a one-dimensional approximation. The new perturbative technique is then applied to the same one-dimensional problem in order to verify the validity of the perturbative approach. It is advantageous to use a monodimensional model to grossly describe the system behaviour, to preliminarily estimate the most important parameters, and to verify the confidence of the perturbative approach. Afterward the flow details are worked out using an axisymmetric approximation (8, 9). Through this model we analyse the fluid-wall interaction, the dynamics of the boundary layer, and the space-time pattern of the wall shear stress.

Particular attention is given to the analysis of the role of the wall elasticity variation $\Delta Eh$ in correspondence of the stent and of the fluid-wall interaction at the junction between vessel and stent.

The flow dynamics is analysed at first in the rigid vessel case, that is when either the vessel and the stent are rigid walls, which constitutes the zero order term of the perturbative method. At second the flow fields are analysed in the case of a uniform elastic wall, and in presence of an elasticity wall variation, respectively $\Delta Eh=0$ and $\Delta Eh=10$.

The enlarged view of upper half vessel profile and the vorticity field during a final stage of the acceleration of the imposed flow is reported in Figure 1.

![Figure 1. Enlarged view of upper half vessel profile and instantaneous vorticity fields at t=9/32 rigid wall case, uniform elastic wall case $\Delta Eh=0$ and elastic wall case $\Delta Eh=10$. Levels from -10.5 to 25.5 step 0.5; negative levels are grey. The dashed line represents the undeformed wall, $e=4x10^{-3}$](image-url)
The boundary-layer develops during the acceleration and separates when a secondary vorticity layer appears, giving rise to a small recirculating cell immediately downstream of the tube enlargement. The separation phenomenon corresponds to the vorticity layer rolling-up and forms a vortex structure travelling downstream.

In the elastic case it can be observed how the vessel is dilated and so it tends to absorb the incoming flow. The walls uniform elasticity, $\Delta Eh=0$, and the vessel motion in phase with the flow pulse work as a smoothing of the field with respect to the rigid case. During the acceleration, the wall synchronous deformation leads to a less extended separated region before the enlargement and to a more intense vorticity (increment of the positive stress) near the narrowing (Figure 1b).

In the case $\Delta Eh=10$ the wall presents the minimum dilatation compared to those with uniform elasticity (Figure 1c) and particularly a profile bump of the vessel.

The distribution of the wall shear stress averaged over a period can be observed in Figure 2.

![Figure 2. Distribution along the vessel of the wall shear stress averaged over a period, the bold line represents the rigid wall case $\varepsilon=0$, others lines represent elastic wall cases with $\Delta Eh=[0 10]$ and $\varepsilon=4\times10^{-3}$](image)

The bold line represents the rigid wall case, the other lines represent the elastic cases.

A constant positive value (Poiseuille-like) of the stress is evident in the first portion of the vessel. We observe a sharp decrease at the enlargement, a positive minimum in $x\sim3$, subsequently an increasing behaviour with a positive maximum peak in $x\sim7.8$ and that is in the portion of the narrowing vessel, then a successive constant linear profile is sought asymptotically after $x\sim10$. The influence of the wall elasticity is marked in presence of a constant elasticity with an increase of the extrema values, while the case with a more rigid stent, $\Delta Eh=10$, is intermediate between the fully elastic and rigid cases.
Additional details of the numerical procedure and results can be found in (9).

The proposed perturbative approach permits to find independently the zeroth order solution, corresponding to the rigid wall case, and the first one afterwards, related to the wall deformation, substantially uncoupling the fluid-wall problem. The method seems able to capture the major features of the wall-fluid interactive dynamics, suggesting the possibility to be applied to the solution of more general, and three-dimensional, problems.

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References

MODELING THE FLUID DYNAMICS OF THE LEFT HEART

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Introduction

During the last years, an increased interest in physically based analyses has been manifested by the medical community, in order to develop quantitative schemes in support to diagnosis and therapy. The main objective is the early detection of pathologies and the refinement of therapeutical techniques.

The scientific activity of the present research teams, in Firenze and Trieste working in close interaction, has been focused on the modelling and understanding of the flow dynamics in the left heart, paying particular attention on the ventricular filling phase (diastole). The diastole represents an intriguing aspect of the heart dynamics, because its role is of fundamental relevance for the optimal functioning of the heart: abnormal behaviours during the diastolic phase represent early symptoms of most heart’s dysfunctions and therefore its improved understanding allows an improved early detection of potential disease (1).

The technological development of the clinical diagnostic tools (Doppler, Echography, MRI, SPECT) has improved the quantity and the quality of data that can be measured in the clinical practice (2). However most clinical indicators that are routinely used for diagnosis do not have a clear correspondence or explanation in physical terms. The accurate modeling of the flow dynamics and of the flow-tissue interaction permits to build interpretative schemes to clinical observation and improve the understanding and control of the involved phenomena.

Methods

The studies are developed by numerical and computational methods. The left ventricle is assumed to have a moving geometry of a truncated prolate spheroid; the internal three-dimensional fluid dynamics is simulated by a highly accurate mixed spectral (along azimuthal direction) - finite difference (on the meridian plane) method written on a boundary-fitted system of coordinates. The flow enters from the mitral plane, in agreement with the ventricle volume variation, with a prescribed velocity profile. The most appropriate mitral velocity profile is evaluated by a separate study centred on the properties of the transmitral jet. The transmitral fluid dynamics is analysed as that through an orifice, with the appropriate, possibly moving, geometry, that separates two chambers. This system is simulated by a finite volume method that allows the proper irregular valvular geometry. In both studies the input parameters, that are the system forcing, are extracted from sets of clinical data supported by the collaboration with cardiological units. The data are generally obtained from non-invasive diagnostic techniques (echo and echoDoppler, B-mode, M-
mode), and recorded in a digital format. The development of techniques of image analysis and post-processing is also a part of the research activity whose objective is to extract objective quantitative physical data from the routine medical measurements.

Results

One realistic example of the flow rate, entering into the left ventricle during diastole and exiting through the aorta during systole, is shown in figure 1 for a healthy tall athlete; this graph is a result of post-processing several M-mode echographic images. The inflow shows two maxima in correspondence of the early filling phase (E-wave) and to the atrial contraction (A-wave) that precedes the systolic ejection (S-wave).

![Figure 1. Left ventricular in/outflow [m²/s] in a healthy subject](image)

The corresponding ventricular flow field shows the presence of a vorticity-wake generated from the mitral orifice (3-5). The role of this intraventricular vortex structure is still debated. After its generation the vortex translates toward the apex for self-induced velocity as it is observed in transmirtal M-mode Doppler measurement commonly performed during the clinical routine (2, 4). The presence of the vortex appears to induce an anticipated closure of the mitral valve that reduces the amount of regurgitation at the beginning of systolic contraction (3). The vortex also has a strong interaction with the ventricle walls (the peak transmitral velocity is about 1m/s and the ventricle is a few cm long) either changing the pressure field, and producing a strong irregular wall shear stress distribution when approaching the tissue (6). One instantaneous vorticity field on one meridian plane (the vorticity component normal to such plane is shown) is reported in grayscale on Figure 2, the valvular orifice is very slightly non-centred and the field is likewise. The relative position of the mitral orifice plays a fundamental role in the three-dimensional geometry of the flow (7), especially in the generation of a return flow that may facilitate the following expulsion through the aortic valve.

The numerical results, when given with the same representation used in clinical routine, compare well with the corresponding medical images; the modelling well reproduces some of the fundamental flow properties while other features are still not included.
A synthetic representation in terms of vorticity vector field is developed. This evidences the differences in the intraventricular flow patterns depending on the valvular geometry and on the tissue dynamics.

**Conclusion**

Several properties of the intraventricular diastolic flow field are reproduced by a numerical model. The existence of a fully controlled model permits the detailed analysis of the physical phenomena related to the fluid and fluid-tissue interaction, particular relevance being taken by the vortex-dominated features. The results allow a quantitative physical interpretation of some clinical data and the improved understanding of modification related to the different pathologies.

**References**

A HYDRODYNAMIC PROBLEM RELEVANT FOR HUMAN VITREOUS DYNAMICS

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Introduction

The vitreous body exists both as a gel and as a liquid and it has a structure formed by a connective tissue interlay. From the mechanical point of view it is a viscoelastic matter whose characteristics depend of age and are variable within the vitreous cavity (Lee et al., 1992). With advancing age the vitreous often loses its consistency and undergoes a liquefaction process. Little is known about the hydrodynamics of the vitreous during ocular movements, both in physiological conditions and in the presence of particular diseases. As far as we know, the only existing attempt to study the dynamics of human eye is due to Coquart et al. (1992) who have developed a finite difference model to study the influence of intraocular pressure on the natural frequencies of vibration of the ocular globe.

Particular intraocular processes, such as inflammations and haemorrhages, may lead to the formation of membranes within the vitreous, which split the vitreous body into separate regions (Figure 1a,b).

![Figure 1. Membrane which separates gel from liquefied vitreous (a); membrane and retinoschisis (damaged retina) (b)](image)

It is customary to classify membranes according to the following criterion: i) membranes surrounded by gel, ii) membranes surrounded by liquefied vitreous and iii)
membranes separating gel from liquefied vitreous. Membranes do not necessarily represent a dangerous medical report; indeed they may form in the vitreous cavity without causing damages to the retina or sight reduction. However, membranes may produce retinal lesions of a diverse nature if they are attached to the retina and they exert tensions on it. Such tensions may arise from a progressive contraction of the membrane (static tensions) or may be generated by the eye movements (dynamic tensions).

In the present contribution we study the effect of eye rotations on the dynamics of a membrane surrounded by liquefied vitreous. In particular we consider saccadic movements of the eye which are characterised by small angles of rotations (lower than 1°) and high frequencies (greater than 10 Hz) (see for instance Findlay, 1971).

**Description of the mathematical model and results**

We study the two-dimensional flow of a fluid within a cylindrical container subject to periodic rotations about its axis. A sketch of the geometry under consideration is shown in Figure 2.

The interior of the cylinder is divided into two equal regions separate by a stretched, elastic membrane; the two ends of the membrane are fixed at the container walls. Referring to Figure 2, the unperturbed position of the membrane is identified by the Cartesian axis $x$ which, at time $t$, forms the angle $\beta(t)$ with the fixed axis $X$. We consider an incompressible, inviscid fluid and assume the irrotationality of the flow field. Moreover, we assume the $X-Y$ plane to be horizontal, hence gravity does not play any role in the analysis.

The assumption of irrotational flow allows us to introduce a velocity potential defined as $\nabla \phi = u$, where $u$ is the fluid velocity. Obviously the velocity $u$, relative to a frame rotating with the circular container is not irrotational as $\nabla \times u = (0, 0, 2\Omega)$, where $\Omega = d\beta/dt$ is the angular velocity of the reference frame. We formulate the problem in an absolute reference frame in terms of the time dependent coordinates $x$ and $y$ as shown in Figure 2. The velocity potential $\phi$ must satisfy the Laplace equation; at the curved side wall we impose the no flux condition and at the membrane the requirement that the membrane is a material surface. The pressure enters the problem through the Bernoulli’s theorem. The displacement of the
membrane in the direction normal to its unperturbed position is described by the variable \( \eta(x,t) \), as shown in Figure 2.

To complete the formulation of the problem we need to introduce a further equation describing the motion of the membrane. The latter is coupled with the flow field through the existence of stresses acting on the membrane, which are in turn determined by the motion of the membrane. The study of one-dimensional oscillations of a membrane, i.e. of a string, is a classical problem (see for instance Courant & Hilbert, 1937). In the present paper we consider a homogeneous membrane. Moreover, we assume that the stretching force \( T \) acting on the membrane is large enough to neglect the direct effect of the container rotations on the membrane movements. This means that the container oscillations are felt by the membrane only through variations of the fluid stresses on the membrane itself. Finally, we assume small oscillations of the membrane about its undisturbed position (the \( x \) axis).

We consider small-amplitude periodic rotations of the container. We then linearise the problem expanding all variables in terms of the small parameter \( \delta \) (representing the amplitude of the container rotations) and keeping in the equations only terms of order \( \delta \). The linearised problem is solved numerically using a second order finite difference scheme. We focus our attention on odd Fourier modes of oscillations of the membrane, which are those forced by the container rotations.

In Figures 3a,b a typical flow field is shown, in terms of absolute and relative velocity, respectively. Figure 3b shows that the relative velocity generates a circulation cell, with an opposite sense of rotation with respect to the container oscillations.

![Figure 3. Typical velocity field, (a) absolute velocity, (b) relative velocity with respect to a reference frame rotating with the container](image)

As it might be reasonably expected, the amplitude of the membrane oscillations is strongly affected by the stretching force \( T \) acting on it. Unfortunately no systematic measurements of \( T \) are yet available in the literature. In the following we will show how the results depend on the ratio between the membrane weight \( P \) and the force \( T \). It is worth noting that, in the context of the present linear analysis, the tension acting on the membrane remains unchanged during membrane oscillations.
In Figure 4a the amplitude of membrane oscillations is plotted versus the ratio $P/T$. It appears that resonant excitation of membrane oscillations may occur for frequencies of eye rotations which are typical of saccadic movements (in the Figure we have used $\omega_0=15$ Hz) and for relatively low values of the stretching force $T$. This result confirms that stretched membranes attached to the retina represent a dangerous medical report.

Finally, in Figure 4b the dimensionless natural frequency of oscillations of the membrane (scaled with the frequency of eye rotations) is plotted versus the ratio $P/T$. The figure shows that $\omega/\omega_0$, strongly decreases as the stretching force $T$ acting on the membrane is decreased. In the figure the dimensionless frequency of oscillation of the membrane in the absence of fluid is also reported (dotted line). It is evident that the presence of the fluid crucially affects the natural frequencies of the system also at the linear level. In particular the presence of the fluid within the vitreous cavity induces a significant lowering of the frequencies of oscillations.

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References

ST JUDE HP BILEAFLET PROSTHESES: A SURVEY ON THE DETERMINATION OF THE EFFECTIVE ORIFICE AREA AND ON THE ANALYSIS OF THE PRESSURE RECOVERY IN STEADY STATE CONDITIONS

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Introduction

The Effective Orifice Area (EOA) is one of the parameters used for the hemodynamic evaluation of the native and prosthetic cardiac valves. The prosthetic heart valves, currently implanted, are analysed either in steady or in pulsatile conditions to quantify the parameter under investigation. One of these methods is based on the analysis of the pressure recovery, which is the typical distribution of the pressure drop downstream of any concentrated hydraulic loss: actually, a prosthetic valve can be regarded as a concentrated hydraulic loss. This phenomenon is due to the interchanges between kinetic and potential energy, but the recovery of the pressure downstream is not complete so, when the pressure reaches a plateau, it is possible to measure a pressure drop, characteristic for each valve given its fluidodynamical conditions, between two given sections, one upstream and the other downstream of the region in which the pressure recovery effect occurs (1). Three different St Jude valves (TAD = 19-, 23-, 27 mm HP model) were studied in steady state conditions, characterizing their hydrodynamical properties; thus, PHV’s local flow structure and global hemodynamical parameters were related, in order to improve the description of these devices’ performance.

Materials and methods

These valves were tested in a mock circulatory loop in steady state conditions, using water as testing fluid; several flow rates were imposed, ranging from 5 to 35 l/min, to analyse the pressure recovery of these biomedical devices and to determine the EOA for all of them (2).

A steady-flow apparatus was built, in which the flow was driven by a constant head tank; the pressure was measured along 17 equispaced taps ($\Delta x = 17.5$ mm) placed on a plexiglass test chamber (diameter = 35 mm), by means of visual inspection of the height of the water column above each pressure tap; the precision of the measurements can be conservatively quantified to be on the order of 0.5 mm of fluid, thus the uncertainty on pressure measurements was 0.037 mmHg. The flow was measured with an electromagnetic flow probe (±0.1% accuracy). The pressure measurements so collected were interpolated by cubic splines in order to estimate the maximum pressure drop at vena contracta.

The basic hypothesis of the two methods here presented (-1- nozzle-like equivalent model of the valve, -2- application of the continuity equation) for the estimation of the EOA, assumes that the dissipation between the section upstream the prosthetic valve and the vena contracta section is negligible; in this way it can be assumed that the pressure drop, characteristic for each valve, is entirely due to the subsequent deceleration of the fluid. With
this assumption the pressure loss can be approximated by the loss relative to a sudden expansion (3) (nozzle-like method). This quantity is normalized by the mean dynamic pressure in the test chamber downstream of the valve:

\[ \zeta = \frac{\Delta p}{\frac{1}{2} \rho v_{aorta}^2} \]

where \( \Delta p \) is the transvalvular pressure drop after the pressure is recovered, \( \rho \) is the density of the water and \( v_{aorta} \) is the velocity in the section of the circular test chamber where the pressure is recovered.

For an axial symmetric sudden expansion the expression for the coefficient \( \zeta \) is

\[ \zeta = \left[ \frac{d_{aorta}}{d_{EOA}} \right]^2 - 1 \]

where \( d_{aorta} \) is the diameter of the test chamber section.

A second approach to the determination of the EOA is given by the application of Bernoulli’s equation; it is possible to estimate the EOA by means of continuity equation

\[ A_i \cdot u_i = A_{EOA} \cdot u_{EOA} \]

where \( A_i \) is the area and \( u_i \) is the mean velocity in the corresponding section - \( i = \) aorta, EOA, \( u_{vena contracta} \) is provided by the Bernoulli’s equation, having determined the pressure at the vena contracta.

**Results and discussion**

An interpolation of the pressure drops, for each valve, in the range 5÷35 l/min has been done with a second order polynomial, of the form \( \Delta P = \alpha \cdot Q^2 + \beta \cdot Q \) under the assumption that the pressure drop across the valve is zero when the flow rate is zero.

The application of these two methods allowed to compare the results of the estimated EOAs for the valves under study; in Figure 1 these estimations are plotted for all the investigated values of flow rate.

![Figure 1. Estimated EOAs values for the three St Jude HP prosthetic valves according to the two proposed investigation methods (curves without circles = nozzle-like method; curves with circles = continuity equation method)](image_url)
The measured pressures follow very closely a law of the type $\Delta P = \alpha \cdot Q^2 + \beta \cdot Q$, on the basis of the fact that the first order term at the right-hand side accounts for the conversion of potential to kinetic energy in the fluid travelling across the valve, while the second order term accounts for viscous losses (4).

Two methods were compared in the determination of the St Jude PHV’s EOA. It is interesting to remark that these two approaches do not use the same data: in the nozzle-like method the total transvalvular pressure is considered, whereas in the approach exploiting the continuity equation to derive the EOA (as also in the Gorlin equation) the maximum transvalvular pressure is used.

Conclusions

It is apparent how the St Jude HP bileaflet heart valve is characterized by an EOA which is not constant with the flow regime, but tends to increase. This result, although already reported for constant-size orifices, has not been hitherto considered in studies addressing the EOA of prosthetic heart valves. A second result is that the two methods here considered, based, respectively, on the nozzle-like model and the continuity equation, give slightly different results, with an increasing difference for larger-size valves. For the 19-mm SJ HP, it is demonstrated that the two methods are equivalent, and probably the measurement relying on the continuity equation can be preferred, due to its simplicity. In the authors’ intentions, the presented results will contribute to an improvement of the current protocols of noninvasive valve area measurements, by incorporating the information relative to the HP’s EOA variation over the considered range of flow rates.

References

Second session

Collaborations

Chairman
Gianni Pedrizzetti
FRACTAL DIMENSIONS ANALYSIS OF EXPERIMENTS IN FETAL SURGERY

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Introduction

Fetal cardiac surgery is actively being studied worldwide as a prospective clinical praxis, capable of providing the treatment of congenital cardiac malformations as early as possible. In fact, in utero interventions could allow the surgical treatment of primary lesions and the prevention of secondary ones, with predictable better outcomes with respect to the results obtained by the application of neonatal and infant repair techniques (1). Previous works (2-4) demonstrate the technical feasibility of fetal cardiac bypass and cardiopulmonary bypass, the greatest obstacle being represented by the progressive loss of placental functionality, especially during the post-bypass recovery. The low fetal flow conditions and the natural extracorporeal membrane oxygenator effect of the residual pregnancy help the anatomic and functional recovery of the fetus.

The aim of our research is to develop new methods of monitoring the biomechanics of the ventricle during a cardiac surgery intervention, as well as the quality of the employed circulatory assistance. This kind of analysis will be beneficial from the standpoint of the post-operative recovery.

The necessarily invasive experimental protocol was described in detail in previous works (5), where the opportunity was underlined of a suitable anestesiological control. In the cited work, the fetal-placental reactivity was studied to the prolonged cardiac bypass. The possibility will be shown that useful information about the contractile state of the ventricle and, consequently, about its recovery, can be obtained by means of a nonlinear analysis of the left ventricular pressure, based on the fractal dimension concept. This analysis could be used in conjunction with other, more traditional types of analysis, such as the end-systolic pressure-volume relationship (ESPVR), already employed in [5] to evaluate the recovery of the ventricular contractile state after steady-flow support.

Materials and methods

The animal model of fetal surgery was the ewe’s fetus. Two cases were selected to show the outcome of a prolonged extracorporeal circulation (ECC) procedure by means of steady-flow assistance. The ECC duration was 60 min., much longer than previously reported in literature (4).

The anesthesia protocol, which has been identified as a major factor in the outcome of the experiments, has been already discussed in (5). The cardiac bypass circuit used in our experimentation was studied to minimize the withdrawal of fetal blood during cannulation, needed to fill the circuit itself. No exogenous priming solution was required.
The left ventricular pressure was measured with a Millar pressure transducer, mounted on a catheter tip. The experimental protocol was as follows: after the instrumentation of the animal, the baseline recordings were performed. The cannulation and ECC set up was then carried out. Afterwards, a 60-min. bypass at high flow rate. At the end of the circulatory assistance the cannulae were removed, blood priming volume was reinfused, and a 90-minute observation period followed.

The left ventricular pressure was analyzed by means of the estimation of the fractal dimension, according to the method of Grassberger and Procaccia [6], indicated for the analysis of single-variable temporal series.

Denoting by \( x(t) \) the signal whose fractal dimension is to be calculated, the set of points defined as
\[
\xi_i = \{ x(t_i), x(t_i + \tau)...x(t_i + (m-1)\tau) \}, \quad i = 1,2,...N, \tag{1}
\]
where \( \tau \) is an appropriate delay, constitute a geometrical object which is embedded in the \( m \)-dimensional phase space.

The dimension of this object, then, will be smaller than \( m \). Denoting the correlation integral as
\[
C(l) = \lim_{N \to \infty} \frac{1}{N^2} \sum_{i,k=1}^{N} \theta \left( l \right) \theta \left( \xi_i - \xi_k \right), \tag{2}
\]
where \( \theta(x) = 1 \) for \( x > 0 \) and \( \theta(x) = 0 \) otherwise, it can be demonstrated that, for small values of the distance \( l \), \( C(l) \propto l^v \). The exponent \( v \) can be considered as the fractal dimension of the constructed set of points in the phase space.

The delay \( \tau \) was chosen so as to obtain a moderate degree of correlation between the components of the vectors \( \xi_i \).

The phase space’s dimension was set to \( m=3 \). As will be seen in the Results, this is higher than what is strictly required for the calculation of a fractal dimension (i.e., \( m > v \)).

In order to have a more general estimation scheme, we considered more than a single fractal dimension. Thus, a pair \((v_1, v_2)\) of fractal dimensions was calculated, \( v_1 \) (\( v_2 \)) being the slope of the regression line relative to lesser (higher) distances \( l \) in the phase space. The cut-off distance \( l' \) marking the separation between the low- and high-distance regions was found by maximizing the sum of the correlation coefficients relative to the linear approximations of \( C(l) \).

**Results and discussion**

Figure 1 reports the results of the analysis for the experiment A, at baseline conditions, during the extracorporeal circulation (ECC), and at three post-ECC phases. Figure 2 provides the same informations for the experiment B. In evaluating these results, it must be remembered that, in the experiment B, the type of anæsthesia had been of difficult control at the start of the experiment (5). Instead, in the other experiment (Figure 1), there was no evidence of this occurrence.
The effect of the ECC phase on the dimension of the relative attractor is evident in case B, where lower values of both correlation exponents $n_1$ and $n_2$ were found with respect to the baseline. On the other hand, a much lesser effect, if any, was found in case A. Since the “baseline” condition is actually the state after the anesthesia delivery, the comparison of this phase in Figure 1 and 2 shows that there is a possible positive correlation between the fetal stress (and the consequent release of agents capable of increasing the ventricular contractility) and the values of $n_1$ and $n_2$.

The proposed generalization of the usual single-dimension analysis proved to be effective in tracking the evolution of the ventricular contractility in the considered experiments. The method does not require very long data segment; thus, it could also be used to monitor in real time the heart’s conditions.

References
REAL TIME CONTRAST ECHO:  
THE NEED OF VENTRICULAR WALL TRACKING  
TO QUANTIFY THE REGIONAL PERFUSION

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Background

Intravenous contrast agents have provided the opportunity to clinically assess myocardial perfusion using ultrasound. In perfusion echocardiography, obtaining maximal diagnostic information requires the use of digital image post processing techniques, since subjective visual interpretation can be frequently inaccurate.

Crucial for an adequate quantification of the contrast signal is the ability to follow the systolic and diastolic movement of the heart walls. With the respect of the ultrasound probe, the heart show not only inherent movement but also displacements due to respiration. Moreover, the physician performing the examination can move the probe itself during the acquisition of the data. For these reasons, if we try to register the signal from the wall utilizing a region of interest (ROI) placed at a fixed location, frequently, the ROI fall on other structures (like left or the right ventricular cavities or outside the heart). Only if the wall is continuously tracked we can extract the signal originating from the tissue and so extract quantitative parameters of regional perfusion.

Currently, the quantification of wall-related properties is performed simply by analyzing the properties within a ROI selected well inside the myocardial tissue and we must verify that the selected ROI remains inside the tissue in all the images of the sequence otherwise information that do not pertain to the tissue are included and the analysis is corrupted. In this way the sequence should be reviewed frame by frame: when the ROI falls outside the tissue it must be moved manually. It is evident how such an approach is inherently extremely time-consuming (in real-time study we must review up to 200 frames for each ROI). Some software application (based on standard edge detection algorithm or on cross-correlation alignment methods) can execute automatically this procedure. In most cases however, these technique do not guarantee the accuracy of the results because they incorporate no information about the structure and the geometry and the wall detection must be still verified manually.

We describe a novel method that allows to continuously tracks in time the myocardial wall and analyze the time evolution of the videointensity in correspondence of the detected wall.

Methods

The loop of images is automatically processed. The central axis of the myocardial wall is determined by an advanced image processing technique that allows recognizing the coherence of the image in a space-time domain, in the same manner the thickness of the wall is detected
by a rigorous statistical approach that defines the dispersion of coherence close to the previously found midline. Such a technique defines the position and thickness of the wall at each instant and allows following its movement. The region of interest becomes a moving one and the analysis is not restricted to a group of points fixed in space rather to points that continuously identify and follow the correct tissue area. Once the myocardium region is systematically determined, at each instant, the signal intensity of the points that belong to such area is averaged and smooth myocardial signal intensity is obtained without the introduction of any artificial smoothing procedure. This signal is then analysed.

First the flash period is automatically determined, and then a non-linear fit to the single exponential function is performed in two steps. A preliminary value of the peak is taken from the pre-flash, when it exists, or from the final part of the signal otherwise, and the corresponding refilling time is obtained from a standard least square procedure in semi-logarithmic space. Subsequently, a least square error minimisation procedure is started to eventually converge to the optimal peak and refilling time parameters of the exponential fitting function.

The procedure here outlined is fully automated, the human intervention is limited to the initial definition (drawing) of a polygon that contains the myocardium at any time, and errors are essentially related to the image quality only.

Results

An example of different quality of curves obtained with a traditional method (A) and with a new method (B) is shown in Figure 1.

![Figure 1. Comparison between the traditional (A) and the new method (B) of regional perfusion quantification](image-url)

The suggested method allowing an automatic detection of contrast refilling curves might increase our confidence with quantitative assessment of myocardial perfusion by contrast echocardiography and has great potentials for the routine use of this new technique.
LAGRANGIAN DESCRIPTION OF FLOW FIELD THROUGH AN AORTIC HEART VALVE

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The advantage of Lagrangian description of a physical phenomenon is to immediately highlight seeding particles time displacement. This lets consider particles mixing between different parts of the test section. Eulerian analysis of velocity field allows to trace instantaneous structure of particles motion. It denies information about particles moving, when they pass through a point of the test section instead of another. Problems related to Lagrangian description, on the contrary, involve characterization of flow field, since it follows particles through entire interesting time interval. That means, in attendance of great local pressure and velocity gradients, such those created by an artificial heart valve, the presence of all the fluid dynamic behaviours belonging to each particles passing through test section, during analysed time interval. This prevents overall view of phenomenon. On the other hand, being able to follow particles for a long time, gives a complete description of occurring events.

This study attempts to characterize artificial aortic heart valve behaviour, during whole left cardiac cycle, tracing pathlines. They were obtained processing subsequent frames. The method proceeds by individuating centres of gravity of particles and than looking for centres referring to the same particle during time evolution. This is obtained using external information about maximum displacement and maximum acceleration (Cenedese and Querzoli, 2000).

In order to make easier the individuation of the trajectories, their density (N) must satisfy condition related to images area (A), maximum velocity (Uₘ) and time separation between frames (Δt):

\[ N < \frac{A}{UₘΔt} \]

The experimental setup consists in an infrared diode laser (Quanta - Milan), output power till 12 W, an infrared sensitive camera (Redlake - USA), set to 1000 frame per second acquisition and 1/2000 shutter opening, an acquisition card connected to PC to download images and the left heart pulse duplicator originally proposed by professor Black (Drury et al., 1989) and properly modified (Grigioni et al., 2000). System was set to an heart rate of 70 bpm and an imposed stroke volume of 1 l/m with a mean aortic pressure of 100 mmHg. Characteristic adimensional numbers related to these setting parameters were Re₁, Rif=3214 and Wo₁, Rif=10.6 calculated considering Uₘ=0.626 m/s (maximum instantaneous velocity averaged on flowmeter section), ν=3.7 cSt (blood cinematic viscosity) and D=19 mm (aortic valve diameter and reference length for adimensionalization). Test fluid was a water – glycerine solution about 33% and seeding particles were a basic anion exchanger (50 – 150 µm diameter).
Cardiac cycle was ideally divided into three parts as suggested by ventricular – aortic pressure signals: systolic flow increasing (132 to 165 ms from cycle beginning), first systolic flow decreasing (165 to 200 ms) and reduced ejection (200 to 340 ms). Any phase was characterized by dividing different trajectories depending on their entrance abscissa (leaflets positions). Trajectories traced in Figures 1 and 3 contain particles coming from back surface of the leaflets, near to the valve ring, and Figures 2 and 4 from top surface, near to the duct centre. This division allows characterization of mass exchange between jets, when particles depart from axial direction.

During acceleration phase of systole, particles proceed parallel to axial direction, neglecting fluid mixing between the three jets outgoing from valve. Furthermore fluid does not separate from walls, because of high temporal pressure gradient (pressure varies from 0 to 27 mmHg) and limited value of Reynolds number. As a result jets seem to be clearly divided one another. After the systolic flow peak is reached (Figure 1 and Figure 2), high values of Reynolds number (3214) let the fluid separate from wall near aortic sinus. Vortex
growing reduces space leaved for fluid flowing. Particles crossing valve near to sinus can now directly flow to outlet section or to be involved in vortex rotation: in the first case, as it happens to particles passing from the centre of the duct or from the sinus opposite side, they will be driven far away from sinus location \((x/D = 1.4 – 1.6)\). Vortex core position changes while pressure drop vanishes, starting from valve ring to Valsalva sinus centre. Otherwise jet mixing becomes visible, with particles deviation from axial direction.

Figure 3 and Figure 4 refer to reduced systolic ejection; sinus located vortex dimensions are smaller than during former phase, due to lower valve outlet velocities. Moreover vortex core position remains the same during whole phase. Particles now show up increased tendencies to mix each other. Reynolds number is lower than in other phases and ventricular – aortic pressure drop is nearly constant.

Pathlines tracing offers chance to understand what particles undergo if an artificial valve is placed instead of a natural one. Thinking to particles as blood red cells, their history gives idea about order of magnitude of cells stresses due to accelerations and velocity direction changes, whether as a consequence of time dependent pressure drops or spatial pressure redistribution.

References


A BOUNDARY INTEGRAL EQUATION APPROACH FOR FLUID-WALL INTERACTION IN ARTERIAL VESSELS

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Introduction

The flow of a fluid in a compliant tube has received much attention because of its relevance in the applications, in particular in biomechanics. Specifically, the fluid-structure interaction is of the primary interest in modelling blood flow, because of the arterial wall remodelling process and subsequent altered flow pattern in pathological states. The fluid and the arterial vessel where it flows, constitute an intrinsically coupled system. Its dynamics is adequately described by a set of differential equations which should be solved by a fully coupled method.

A boundary integral method will be used here to solve the blood-vessel system and will be adapted for the specific features of the problem at hand. Boundary integral methods have been extensively used in solving the interaction of elastic boundaries with external flows in aeroelastic and acoustoelastic problems. The main advantage of such a formulation stems from the redefinition of a tridimensional differential problem into an integral form defined on a 2D manifold (the domain boundary) embedded into the 3D space. This results in a reduction of the computational effort required for the numerical solution of the coupled system. Such a technique provides the description of the dynamics of the flow pattern around a solid elastic structure and gives useful information about the critical conditions assuring flow-structure stability. In this preliminary work, we will confine to the small perturbations both for the elastic displacement and for the fluid velocity.

The main objective of this study is to get insight of the complex relationship between arterial pressure, wall deformation and flow field in wave propagation phenomena and their modification in presence of a prosthetic implantation or in a pathological condition.

Mathematical formulation

In this work we assume the blood as an incompressible and inviscid fluid. This approximation is acceptable in large vessels, where the diffusion effects are secondary and the boundary layer thickness is typically negligible with respect to the lumen radius, and the velocity profile is constant along the arterial section. Under these assumptions, an initially irrotational flow remains irrotational at all times, and the velocity field may be described in term of a scalar potential $\phi$, such that

$$v = \nabla \phi \quad \forall x \in V \quad [1]$$

where $V$ represents the volume enclosed in the arterial district under consideration, bounded by the surface $S$. The latter is considered as the union of the surfaces $S'$ and $S''$. 

59
corresponding to the input and output sections of the flow field, respectively, as well as the surface $S^w$, representing the distensible arterial wall (Figure 1). Note that $S^i$ and $S^o$ are fictitious surfaces introduced for numerical purposes.

![Figure 1. The domain under analysis](image)

The elastic motion of $S^w$ is the responsible of the fluid-structural coupling that will be analyzed in Section 3. The equations governing the flow are the Laplace equation for $\phi$

$$\nabla^2 \phi = 0,$$

and the linearized Bernoulli’s equation, $p = -\rho \dot{\phi}$, which gives the relationship between pressure and velocity potential (assuming zero reference pressure). The above equations have to be completed by suitable boundary conditions [4]. To do this, we have to distinguish the role of the different surfaces introduced above: if $x \in S^i$ the inflow is assumed to be a known function of time (typically periodical), whereas for $x \in S^w$, the impermeability of the arterial wall is imposed. The boundary conditions on $S^o$ depend on the solution of the flow. An expression relating the outflow to the Cauchy data on $S^i \cup S^w$ may be obtained by imposing a zero total flux on the boundary of $V$. Thus, the Neumann-type boundary conditions associated to Eq. 2 are

$$\frac{\partial \phi}{\partial n} = v^i \cdot n \quad \text{for} \quad x \in S^i$$

$$\frac{\partial \phi}{\partial n} = v^w \cdot n \quad \text{for} \quad x \in S^w$$

completed by the compatibility condition

$$\int_{S^i} \frac{\partial \phi}{\partial n} \, dS = \int_{S^w} \frac{\partial \phi}{\partial n} \, dS + \int_{S^r} \frac{\partial \phi}{\partial n} \, dS + \int_{S^c} \frac{\partial \phi}{\partial n} \, dS = 0$$

Note that $v^i$ in Eq. 3 is a known function of time, whereas $v^w$ in Eq. 4 represents the velocity of the arterial walls due to elastic deformation. Using the standard procedure (see [3] for details), Eq. 2 may be recast in the integral form

$$\phi(y, t) = \int_{S^i} \left( G \frac{\partial \phi}{\partial n} - \phi \frac{\partial G}{\partial n} \right) \, dS$$
where \( G = -1/4\pi |x - y| \) is the fundamental solution of the Laplace equation. When the observation point \( y \) is in \( V \), Eq. 6 gives the value \( \phi(y, t) \) as a function of the distribution of \( \phi \) and \( \partial \phi / \partial n \) on \( S \). On the other hand, if \( y \in S \), Eq. 6 represents an integro-differential equation, which can be numerically solved by a Boundary Element Method (BEM).

**Numerical discretization**

The numerical solution of Eq. 6 is obtained using a zeroth-order BEM: the boundary \( S \) is divided into \( M \) quadrilateral elements, \( M \) collocation points are located at the centers of each panel, and the functions \( \phi \) and \( \chi = \partial \phi / \partial n \) are assumed to be element-wise constant.

Approximating the integral in Eq. 6 with the sum of integrals on each element, and taking into account the zeroth-order representation of the variables, we obtain

\[
\phi_k = \sum_{j=1}^{M} [B_{kj} \phi_j + C_{kj} \chi_j] \quad k = 1, \ldots M \quad [7]
\]

where

\[
B_{kj} = \int_{S_j} \frac{-1}{4\pi |x - x_j|} dS, \quad C_{kj} = -\int_{S_j} \frac{\partial}{\partial n} \frac{-1}{4\pi |x - x_j|} dS \quad [8]
\]

Indicating with \( \{\bullet\} \) the column matrix of the values of the variables at the \( M \) collocation points, and separating the contributions of \( S' \), \( S'' \) and \( S''' \), the resulting set of algebraic equations for the \( M \) unknowns \( \phi_k \) may be written in the form

\[
(I - C)\phi = B'\{\chi\} \quad \text{for} \quad k = 1, \ldots M
\]

where the \( (M \times M) \) matrices contain the integral coefficients 8, and \( \{\chi\} \) is known from the boundary condition 3. In the next Section the dependence of \( \{\chi\}'' \) on the wall dynamics will be derived. Here we note that, under the assumption of uniform velocity profile at input and output sections, an expression for \( \{\chi\}'' \) may be derived from Eq. 5. In particular, being \( \partial \phi / \partial n \) constant on \( S' \) and \( S'' \), we obtain

\[
\frac{\partial \phi}{\partial n} \bigg|_{\text{ke}, S'} = -\frac{1}{A'} \left[ \frac{\partial \phi}{\partial n} \bigg|_{\text{ke}, S'} A' + \sum_{j=1}^{M} \frac{\partial \phi}{\partial n} \bigg|_{A_j} A'' \right] \quad [10]
\]

where \( M \) is the number of panels defined on \( S'' \), and with \( A' \), \( A'' \) and \( A''' \) we indicate the areas of the respective surfaces. Recalling Eq. 3, the column matrix collecting the values of the outflow on the panels may be written as

\[
\{\chi\}'' = \{\phi\}'' + G\{\chi\}'' \quad [11]
\]
where $\{\hat{x}\}'$ is known from the inflow boundary conditions. Substituting into Eq. 9 we obtain

$$\left(I - C\right)\phi = B'\{\chi\}' + B''\{\hat{x}\}'' + \left(B''G + B''\right)\{\chi\}'$$  \[12\]

**Fluid-structure interaction**

Here, we consider a purely elastic arterial wall. The general form of the equation governing the dynamics of the vessel may be written as $\rho_w\ddot{u} + L\dot{u} = f$, where $\rho_w$ is the density of the solid wall, $u$ is the elastic displacement, $f - p_n = \rho\ddot{u}$ is the force due to blood pressure, and $L$ is the structural linear differential operator. In this paper, we don’t deal with a particular expression for $L$, focusing our attention on the general form of the fluid-structure interaction mechanism (specific linear or linearized forms for $L$ may be found in [5]). To this aim, we note that the impermeability boundary condition on $S''$ in Eq. 3 may be written in term of $u$ as $\{\hat{x}\}'' = v'' \cdot n = \dot{u} \cdot n$. We now express $u$ in terms of its component on a suitable set of orthonormal functions $\varphi_j(x)$, $u(x, t) = \sum_{l=1}^{\infty} a_l(t)\varphi_j(x)$, and the impermeability boundary conditions assume the form

$$\{\hat{x}\}'' = \sum_{l=1}^{\infty} a_l(t)\varphi_j(x) \cdot n.$$  \[13\]

Truncating the summation to the order $N$, substituting into the equation governing the dynamics of $u$, and using the Galerkin approach we obtain

$$\mathbf{M}[\tilde{a}] + \mathbf{K}[\tilde{a}] = \{\bar{e}\}$$  \[14\]

where $\{\tilde{a}\}$ is the $N$-dimensional column matrix containing the spectral components of $u$, the elements of $\{\bar{e}\}$ and $\mathbf{M}$ are $e_i = \langle \rho\ddot{u}\varphi_i, \varphi_i \rangle$ and $m_{ij} = \langle \rho\ddot{u}\varphi_i, \varphi_j \rangle$, and the form of matrix $\mathbf{K}$ depends on the expression used for $L$. Laplace-transforming Eq. 14 it is possible to derive, after some manipulations, the $(N \times M)$ matrix transfer function relating the spectral components $\dot{\phi}(s)$ of the velocity potential at the collocation points to the harmonic components of $u$, $\{\tilde{a}\}$ (for details, see Ref. [2]),

$$\{\tilde{a}\} = s\left(Ms^2 + \mathbf{K}\right)^{-1}\{\bar{e}\} = \mathbf{H}(s)\{\bar{\phi}\}.$$  \[15\]

Thus, the value of the boundary condition on $S''$ may expressed in terms of the velocity potential using Eq. 13, and introducing the $(M \times N)$ matrix $\mathbf{Z}$ which gives the value of scalar products $\mathbf{u} \cdot \mathbf{n}$ at the collocation points as a function of the spectral components $a_i$,

$$\{\hat{z}'\} = \mathbf{ZH}(s)\{\bar{\phi}\} = \mathbf{Q}(s)\{\bar{\phi}\}.$$  \[16\]

Substituting into Eq. 12 we obtain the final form of the system
\[
\{ \vec{v} \} = (\mathbf{I} - \mathbf{C} - \mathbf{Y}(s))^{-1}\left[ B'\{ \vec{x} \} + B''\{ \vec{q} \} \right] = \mathbf{T}(s)\{ \vec{r} \}
\]  \hspace{1cm} [17]

where \( \mathbf{Y}(s) = [B'G + B''Q(s)] \) and \( \{ \vec{q} \} = [B'\{ \vec{x} \} + B''\{ \vec{q} \}] \) represents the known terms.

In the above equation, \( \mathbf{T}(s) \) represents the matrix transfer function of the system, which relates the Cauchy data set to the harmonic components of the velocity potential. Note that \( \mathbf{T} \) depends on the dynamics of the arterial walls through matrix \( \mathbf{Q} \). Thus, the coupled system is capable to evaluate the velocity field in the domain \( \mathcal{V} \) taking into account the response of the compliant walls. Equations similar to 17 have been successfully applied in the past to the analysis of the acoustic characteristics (i.e., input and radiation impedance) of rigid pipes filled with a compressible media (1). The aim of the present work is to apply the above formulation to simulate the propagation of pulsating signal inside arterial districts. In particular, the effects of variations of the elastic properties of the walls (due, for instance, to prosthetic implantations) will be examined, using special forms of matrix \( \mathbf{H} \).

References
PROSTHETIC HEART VALVES CAUSE MECHANICAL STRESS AND HEMOLYTIC ANAEMIA IN PATIENTS WITH HEREDITARY ERYTHROCYTE MEMBRANE DEFECTS

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Introduction

Heart valve replacement with mechanical prosthesis is frequently associated with chronic subclinical hemolysis so that anaemia is rarely evident (1, 2). Generally erythrocyte damage is more pronounced with malfunctioning than with properly working prostheses (3). Nevertheless, some degree of well compensated hemolysis has been demonstrated in patients with normofunctioning mitral or aortic mechanical prostheses (1-3). In this study two patients with aortic and mitral prosthetic valves affected by severe or mild haemolytic anaemia were investigated. In order to ascertain the cause of the hemolytic state, biochemical investigations regarding hereditary hemolytic anemia were carried out and measurements of viscosity and visco-elasticity were performed.

Patients

Case 1. A 59-year old male with a mitral prosthetic heart valve (Hancock) was affected by severe hemolytic anemia (RBC 2.72x10^{12}/l; Hb 8.4 mg/dl; Hct 0.251; reticulocytes 11.2%) and jaundice (total and unconjugated bilirubin 3.49 mg/dL and 3.20 mg/dl, respectively). Laboratory investigations revealed a decreased value in aptoglobin (6mg/dl) and a marked increase in lactate dehydrogenase (LDH) activity (7300 U/l).

Case 2. A 29-year old female with an aortic prosthetic heart valve (Hemashield 22 mm plus a JM21) was affected by mild hemolytic anemia (RBC 3.12x10^{12}/L; Hb 9.3 mg/dl; Hct 0.265; reticulocytes 2.1%), and splenomegaly. Serum parameters showed a decreased value in aptoglobin (5mg/dl) and a slight increase in LDH activity (520 U/l).

Methods

After informed consent had been obtained, blood samples were drawn by venipuncture, collected on K₂-EDTA and processed within 2-3 hours. Haematological and serum parameters were determined by conventional techniques. Erythrocyte morphology was observed on Romanowsky stained blood. Osmotic fragility was assessed by acidified glycerol lysis test (AGLT₅₀) (4).
The electrophoretic analysis of erythrocyte membrane proteins was performed by polyacrilamide gel electrophoresis in sodium dodecylsulfate (SDS-PAGE; 7.5% acrylamide) as previously described (5). Protein bands were stained by Coomassie Blue and quantified by a Fluor-S MultiImager (BIO- Rad).

The erythrocyte viscosity and viscoelasticity were measured by Rotovisco RV20 with CV100 and ME30 measuring sistems (Haake) (6).

Results

Some abnormalities of erythrocyte morphology were observed on blood smears: the presence of spherocytes in the first case and of elliptocytes in the other one. The AGLT50 values were decreased (132 s and 420 s; normal value >1800 s) demonstrating an increase in erythrocyte osmotic fragility. These findings pointed out the presence of hereditary red blood cell (RBC) membrane defects. The SDS-PAGE electrophoresis of erythrocyte membrane proteins confirmed the presence of a decreased content in protein 4.2 and in spectrin, respectively. So the diagnosis of hereditary spherocytosis (HS) in the first patient and the hereditary elliptocytosis (HE) in the other one was made.

The measurements of blood viscosity (200 s$^{-1}$ and 1 s$^{-1}$) and flow curves (shear stress vs shear rate) showed decreased values in HS and HE patients in comparison with the control ones (Table 1) in agreement with the presence of congenital erythrocyte membrane defects and mechanical prosthesis.

### Table 1. Blood viscosity and visco-elasticity in patients with hereditary erythrocyte membrane defects and prosthetic heart valves

<table>
<thead>
<tr>
<th>Patients</th>
<th>Viscosity 200 s$^{-1}$</th>
<th>Viscosity 1 s$^{-1}$</th>
<th>Flow curve</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case 1 (HS)</td>
<td>2.6 mPa</td>
<td>11 mPa</td>
<td>0.51 Pa</td>
</tr>
<tr>
<td>Case 2 (HE)</td>
<td>3.5 mPa</td>
<td>15 mPa</td>
<td>0.72 Pa</td>
</tr>
<tr>
<td>Control</td>
<td>5.0 mPa</td>
<td>25 mPa</td>
<td>1.0 Pa</td>
</tr>
</tbody>
</table>

Conclusions

Hemolysis is no longer complication of heart valve replacement with mechanical prostheses. The chronic intravascular hemolysis in patients with the new mechanical valves is mild, subclinical and decomposed hemolytic anemia is a rare finding (1). Nevertheless many factors have been found to influence the degree of hemolysis: site, design, size, model and number of prostheses (1-3). This study points out that not only mechanical stress but also the coexistence of a congenital erythrocyte membrane protein defect can induce and make worse hemolytic anemia in patients with heart valve prosthesis.

References


A NEW METHOD FOR THE NONINVASIVE QUANTIFICATION OF HEART VALVE REGURGITATION

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Introduction

The measure of the regurgitant flow through the tricuspid or the mitral valve provides a significant indication of the severity of the valve closure dysfunction, and has a clear diagnostic importance. The estimation of the volume passing through the closed valve during systole, and its ratio with the ejection volume, can significantly improve the assessment of an ongoing valvular pathology. However, the noninvasive quantification of flow converging to the valve is still lacking a satisfying degree of precision. With the present study, a new method is presented of exploiting the information contained in two-dimensional images of the instantaneous flow, such as those provided by the commercially available Color Doppler Echocardiography equipments. These images correspond to digital maps of one component of the flow velocity, which can be readily post-processed by suitable algorithmic routines. Thus, the quantification of the regurgitant flow, based on the analysis of Echocardiographic images, can be made more rigorous by applying the laws of fluid dynamics.

To date, the most popular technique for quantifying the regurgitant flow of a native or prosthetic valve is the Proximal Isovelocity Surface Area (PISA) method applied to Color Doppler Echocardiography images of the flow converging to the valve. The PISA method is based on the assumption of a prescribed flow pattern of a sink type: on this basis, the converging flow rate is estimated only from the axial (vertical) component of velocity. It is well known that this approach often introduces a significant approximation of the actual flow and a relevant error in the estimate of the regurgitant volume. In particular, it relies on the doubtful assumption that the isovelocity surface is spherical. Therefore, even if such a quantification concept can be easily applied (one velocity value and one or two geometric parameters can be extracted and combined by a simple hand computation), its accuracy is rather poor. The present work is meant to improve the PISA-based estimations, since no prior knowledge about the form of the isovelocity surface is required, and the processing is carried out of all the velocity information contained in the Doppler image, thereby yielding an automatic calculation of the valvular regurgitation based on physical principles.

Materials and methods

A two-dimensional instantaneous Doppler image contains the spatial distribution of one component of velocity. Defining a system of coordinates \( \{x,z\} \), where \( z \) represents the
vertical direction and \( x \) is parallel to the valvular plane assumed to be at \( z=0 \), the Doppler image is the map of the vertical component of velocity \( v_z(x,z) \).

The valve is centered at a position \( x=x_0 \), and the velocity field presents an approximate symmetry with respect to valve centerline. Such an approximate symmetry axis can be identified manually during the image acquisition, or automatically in the post-processing stage. The definition of such an axis has a relevance in the subsequent analysis, because only the symmetric part of the velocity field contributes to the evaluation of the flow rate, while the antisymmetric component of velocity provides a null contribution when integrated, and can therefore be neglected. It must also be noticed that a possible non-axisymmetric distribution of velocity cannot be quantified by a two-dimensional image which corresponds to the knowledge of just two points along the circumferential direction. Then, referring to the axisymmetric velocity field obtained by symmetrization of the original data, we can consider a cylindrical system of coordinates \( \{ r, z \} \) where \( r=0 \) represents the symmetry axis of the extracted axisymmetric velocity field \( v_z(r,z) \).

The continuity equation in its differential form, i.e. the principle of conservation of mass applied to any elementary volume of fluid, gives a relation between the axial, \( v_z(r,z) \), and the radial, \( v_r(r,z) \), velocity component: in cylindrical axisymmetric coordinates the continuity equation reads

\[
r \frac{\partial v_r}{\partial z} + \frac{\partial v_z}{\partial r} = 0.
\]  

Integration of this equation along \( r \), starting from the axis where the radial velocity is zero for symmetry reasons, allows the explicit evaluation of the radial velocity

\[
v_r(r,z) = \frac{1}{r} \int_0^r s \left( \frac{\partial v_z}{\partial z} \right)_{r=z} ds.
\]  

The numerical evaluation of this integral provides the radial velocity component with limited computation times.

Once that the complete velocity field is known, the flow rate passing through any axisymmetric surface can be immediately evaluated. From the principle of conservation of mass, written in integral terms, the flow through the valve is equal to the total flow crossing any axisymmetric surface surrounding the valve; indicating with \( \ell \) the imprint-curve of the surface on a meridional plane, the flow rate \( Q \) is given by

\[
Q = 2\pi \int_{\ell} v_n r d\ell;
\]

where \( v_n \) is the projection of the velocity vector in the direction normal to the curve. Unlike the PISA approach, the proximal surface can be chosen arbitrarily; ellipsoidal surfaces will be considered in the results presented below.

*In vitro* testing of the new method was made at the Laboratory of Biomedical Engineering of the ISS, using the VSI LT9891 (Vivitro Systems Inc., Canada) valve leakage tester and the AU3 Partner (ESAOTE S.p.A., Italy) Color Doppler ultrasound system, to collect images of the regurgitant jet, generated with the use of a 2-mm-diameter stenosis, built according to the ISO 5840/ Working Draft #2 (1994). Analysis of the experiment was performed considering different radii of the proximal surface, supposed spherical for PISA, corresponding to isovelocity values ranging between 90 and 98% of the maximum velocity.
This value was chosen as the height of the ellipsoidal surface used by the new method in the flow rate calculations.

Results

*In vitro*, the fixed volume of fluid (170 ml) was forced steadily through the stenosis in 10.7 seconds, resulting in a flow rate of 15.89 ml/s. The flow rate was evaluated with the PISA method using a spherical isovelocity surface and with the new method, using either the same spherical flow surface or two ellipsoidal surfaces with basal radius of 1.5 and 4 mm. Figure 1 reports the estimated flow rates; unlike the new method, the PISA approach yielded a considerable overestimation of the actual flow rate. It should be noted that the mean value of the flow rate measurements provided by the new method was only 0.26% higher than the actual value.

![Figure 1. Comparison between the PISA and the new method for regurgitant volume estimation](image)

Conclusions

The proposed method was found to yield substantial improvements in the accuracy of the calculation of regurgitant volumes in comparison to the standard PISA method, after the analysis of Color Doppler recordings of regurgitant jets. The more rigorous description of the flow field offered by the new method will contribute to a better evaluation of valve function, without resorting to excessive computational effort, resulting in a more reliable basis for diagnosis.
AUTHORS’ INDEX

Abbate, M.; 8
Agati, L.; 54
Auricchio, F.; 13
Baccani, B.; 38
Balducci, A.; 56
Barbaro, V.; 3; 8; 31; 45; 51
Bolzon, G.; 38
Caprari, P.; 64
Carotti, A.; 51
Cianciulli, P.; 64
D’Avenio, G.; 8; 31; 45; 51; 67
Daniele, C.; 8; 31; 45; 51; 67
Del Gaudio, C.; 31; 45; 51
Di Benedetto, G.; 31
Domenichini, F.; 38
Grigioni, M.; 8; 31; 45; 51; 56; 64; 67
Iemma, U.; 59
Martorana, M.C.; 64
Migliavacca, F.; 13

Mojoli, G.; 64
Morbiducci, U.; 31; 45; 51
Nicosia, S.; 26
Padula, M.; 19
Pedrizzetti, G.; 38; 54; 67
Petrini, L.; 13
Pezzinga, G.; 26
Pietrabissa, R.; 13
Pontrelli, G.; 59
Querzoli, G.; 56
Repetto, R.; 41
Romano, G.P.; 56
Salvati, A.M.; 64
Seminara, G.; 41
Tarzia, A.; 64
Tonti, G.; 54; 67
Tortoriello, A.; 34
Zovatto, L.; 38
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