

# Digital Frequency Analysis of Valve Sound Phenomena in Patients after Prosthetic Valve Surgery: Its Capability as a True Home Monitoring of Valve Function

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**Background and aim of the study:** Depending on the individual risk profile of a patient, disturbances of the functional integrity of mechanical heart valve prostheses occur in up to 2.5% of patients each year. The early phase of prosthetic dysfunction (due to thrombus formation, tissue ingrowth or endocarditis) usually remains undiagnosed, as patients do not present with symptoms in this situation, and imaging techniques (echocardiography, fluoroscopy) demonstrate normal occluder motion. The delay between the onset of prosthetic valve dysfunction and its clinical manifestation may result in complications (e.g. thromboembolism) or extended therapeutic options (e.g. reoperation rather than more intensive anticoagulation).

**Methods:** A total of 291 patients with mechanical heart valves was allocated to four different subgroups, and each measured their valve sounds regularly with the 'ThromboCheck' device. Depending on the subgroup, the signals were compared with different reference signals. Patients in whom a suspicious signal was detected were immediately contact-

ed and examined meticulously.

Despite major advances in the treatment of heart valve lesions, there remains a complication rate of between 0.8% and 6% per year for those patients who have undergone valve replacement surgery (1-4). Considering that approximately 100,000 heart valve operations are performed worldwide each year, the number of serious complications related to thrombosis, tissue ingrowth, leaflet tears, calcification, leakage and prosthetic valve endocarditis still numbers several thousand.

A prosthetic, non-structural valve dysfunction which is consistent with disturbed motion of the leaflets caused by thrombus formation or tissue ingrowth

ed and examined meticulously.

**Results:** Fourteen patients were found to have suspicious signals. In 13 patients, valve dysfunction was confirmed by fluoroscopy, but in four cases neither transthoracic nor transesophageal echocardiography detected abnormal occluder motion or 'musses' adjacent to the prosthesis. Normal valve sounds returned in four patients who underwent thrombolytic therapy. All patients regularly recorded and passed on their signals. Surveys revealed high acceptance and easy handling of the Thrombocheck device.

**Conclusion:** Home monitoring of sound pressure measurements of prosthetic valves by digital frequency analysis via a Fast Fourier transformation may detect even very mild alterations of prosthetic valve function. The next evolution of control systems, allowing for registration of flow, frequency spectrum and electrocardiography, opens potential applications for Internet-based, remote monitoring of cardiac patients.

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probably develops over a period of several days to weeks. Prosthetic valve dysfunction is usually discovered only after manifestation of serious fatal events, such as thromboembolic complications or heart failure.

In order to reduce the risk of undiagnosed valve dysfunction between two medical consultations, a system was developed which allows recording of the acoustic phenomena with minimal effort at any place worldwide, and in a manner which is economically acceptable.

As minimal changes in prosthetic valve function were reliably detected by frequency spectra analysis (5-8), this technique has the potential to diagnose dysfunctions long before hemodynamic deterioration or manifestation of systemic complications occur.

Initially, preliminary experience was gained with recording the frequency spectra of the click phenomena of prosthetic valves, their analog/digital processing

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and comparison with a reference file. The encouraging initial results obtained led to the introduction of a first hand-held device (the 'ThromboCheck') for home monitoring of the functional state of prosthetic heart valves.

## Clinical material and methods

This study comprised three aspects: simulation studies, animal experiments, and some clinical investigations, the results of which have been published previously (5-7). Herein are presented the preliminary results of the first multicenter application of the 'ThromboCheck', and the first single-center prospective, double-blind study. After appropriate training for use of the Thrombocheck, four different sub groups of patients were evaluated with the device.

### Subgroup 1 (double-blind, prospective)

Eighty-eight patients (51 males, 37 females; mean age 52.6 years) underwent aortic valve replacement (AVR) (n = 51), mitral valve replacement (MVR) (n = 30), pulmonary valve replacement (PVR) (n = 1), MVR + tricuspid valve replacement (TVR) (n = 2), AVR + MVR (n = 2), and PVR + TVR (n = 2). The valves implanted were St. Jude Medical (SJM; St. Paul, MN, USA) or Medtronic Advantage (Minneapolis, MN, USA), both of which were bileaflet. All patients were provided with the Thrombocheck during their hospital stay for valve replacement surgery. Patients were trained to handle the device in addition to conducting International Normalized Ratio (INR) self-management using the 'CoaguCheck' device. The mean follow up of these patients was  $3.2 \pm 2.1$  months. The results were double-blinded and decoded by an independent supervisor. Registration of the digital frequency analysis of the sound phenomena was encoded; this was transmitted every other day and decoded and controlled by a person unknown to either the patient or to the study center. If the decoded signal demonstrated any suspicious sound phenomena, the study center was informed immediately.

A detailed clinical follow up focusing especially on potential microemboli was performed every three months by means of patient interviews.

### Subgroup 2

A multicenter study is currently investigating whether anticoagulation therapy without coumarin derivatives after implantation of a mechanical valve prosthesis is reasonable. All 30 patients currently involved in the study were provided with a ThromboCheck device and trained in its use while still in-patients after their valve surgery. In contrast to subgroup 1, the results of the digital frequency analysis

are shown in the display of the device with a short message ('ok', error > 'repeat measurement', 2nd error > 'consult your physician').

### Subgroup 3

Five devices were utilized in an application trial in cardiological centers in Israel. In this trial, the patient's frequency spectrum (valve models, all bileaflet, were SJM, CarboMedics, Sulzer Carbomedics (Austin, TX, USA) and Sorin Bicarbon (Sorin Biomedica, Saluggia, Italy) was compared with the 90% percentile of an average frequency spectrum obtained from 50,000 pre-clinical measurements of the frequency and amplitude distribution of click sounds of different mechanical prosthetic valves. At present, 71 patients are involved in this trial, which is on-going.

### Subgroup 4

Another 102 patients (68 males, 34 females; 87 with AVR, 15 with MVR; sinus rhythm in 83%) provided themselves with a ThromboCheck device late after the implantation of a mechanical valve prosthesis (mean  $4.2 \pm 1.7$  years), having been informed of the device's existence via the Internet or self-help groups. The valve types included were mainly SJM and Medtronic Advantage; only two patients had received monocusp valves (Medtronic Hall, Minneapolis, MN, USA). Apart from their prosthetic heart valves, these patients were healthy. Ninety-four (92%) of the patients were INR self-managers. As part of a voluntary interview with regard to their quality of life, the patients were prepared to provide information about the handling and user-friendliness of the device.

## Results

Among the present patient cohort, 14 patients were found to have suspicious sound signals (3.8%), and these were confirmed in 13 cases by using alternative diagnostic methods. In 13 patients a pathological valve function was confirmed by fluoroscopy, while in four cases neither transthoracic echocardiography (TTE) nor transesophageal echocardiography (TEE) revealed a suspicious signal. A normal valve sound returned in four patients after thrombolysis had been carried out.

### Subgroup 1: (double-blind, prospective)

The patients managed the handling and transfer of the encoded data without any problems. Prosthetic valve endocarditis, peripheral or central embolizations were not diagnosed during the entire observation period. Among all of the INR measurements, 87% were within the therapeutic range.

One female patient transmitted a suspicious frequency spectrum for three consecutive days at approx-

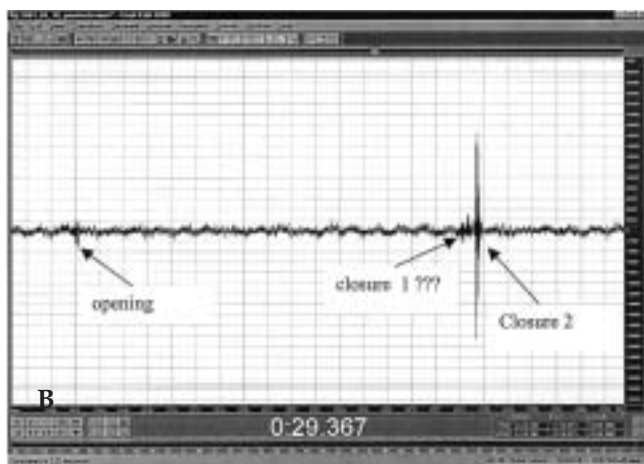
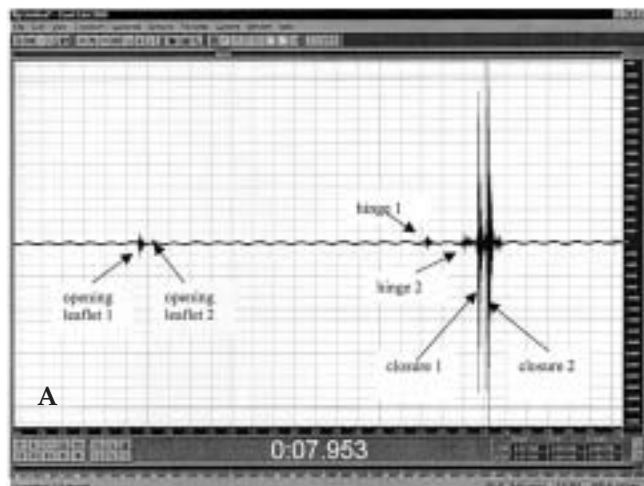


Figure 1: A) Frequency spectrum of a prosthetic valve with regular function. Note the characteristic opening and closure sounds of a bileaflet valve. B) Frequency spectrum of a valve with impaired leaflet motion. Only the opening and closure sound of one leaflet is recorded.

imately six weeks postoperatively. At the same time, the INR values shifted between 1.7 and 2.1 (INR self-management). At one day after the INR had reached the target therapeutic range ( $\geq 2.8$ ), the frequency spectrum was normalized. As the patient remained completely asymptomatic, no further diagnostics were performed.

The vast majority of patients felt that the device was easy to use, reliable, and improved their well-being.

Following a special adaptation of the software, the frequency analysis of patients with two prosthetic valves was found to be reliable, even if they were not in sinus rhythm.

### Subgroup 2

In this subgroup, three patients (10%) presented with a pathological frequency analysis. The device recorded

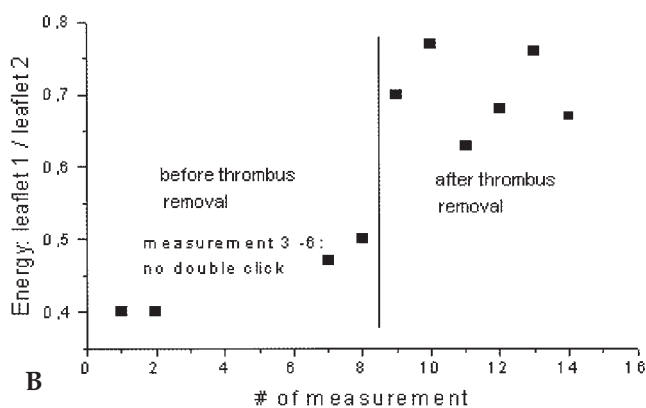
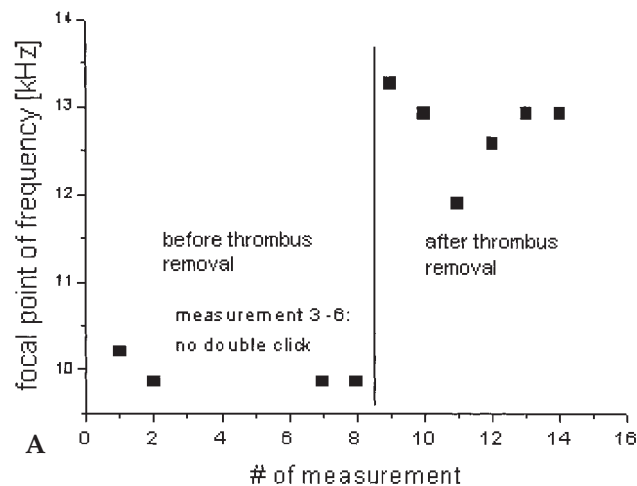


Figure 2: A) Focal point of frequency before and after surgical removal of thrombus. B) Relationship of acoustic energy of the two leaflets before and after surgical removal of thrombus.

two suspicious measurements, leading to a request to consult the physician in each case.

### Subgroup 3

Ten of 71 patients (11%) demonstrated a suspicious frequency analysis during routine check-up. In nine patients an impaired valve function could be demonstrated, and one suspicious frequency analysis was interpreted as a false negative. Four patients with one leaflet stuck at the closed position were admitted for thrombolytic therapy with recombinant tissue plasminogen activator. At 48 h after thrombolysis, three patients again showed an inconspicuous frequency signal (8).

### Subgroup 4

In this subgroup, neither clinical symptoms nor fre-

Table I: Reported patient experiences with the ThromboCheck device (n = 102).

No. of measurements per week	
3-5 times	70.8%
6-8 times	29.2%
Handling	
Easy	100%
Acceptable	-
Complicated	-
With ThromboCheck, I feel...	
Safer	62.5%
Neutral	20.8%
More concerned	16.7%
Technical problems	
No	95.8%
Yes	4.2%
General impression	
Very good	50%
Good	50%
Acceptable	-
Bad	-

quency spectra indicative of prosthetic malfunction were detected during a mean observation period of  $4.2 \pm 1.3$  months. The results of the questionnaire regarding user-friendliness, handling, technical problems and quality of life are listed in Table I.

### Exemplary cases

#### Case no. 1

In this 64-year-old male (who underwent AVR with a bileaflet, On-X, valve), anticoagulation therapy was switched from warfarin plus aspirin to aspirin alone. After three months, the ThromboCheck recorded pathological frequency spectra indicative of impaired leaflet motion for three consecutive days (Fig. 1A). Neither TTE nor TEE identified any pathology. Fluoroscopy confirmed valve dysfunction with incomplete occluder motion of one leaflet. At four days after the first pathological frequency signal had been documented, medication with heparin plus warfarin was started. After five days, the ThromboCheck signals were normalized (Fig. 1B).

#### Case no. 2

This 72-year-old female (AVR bileaflet valve, SJM), stopped oral anticoagulation prior to an orthopedic operation. Several weeks later, the patient consulted her physician because of dyspnea. TEE revealed an impaired motion of both leaflets, without any demonstration of thrombus. Surgical revision of the prosthet-

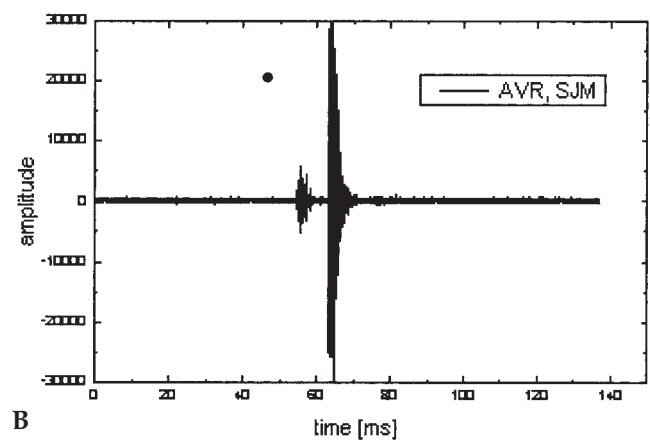
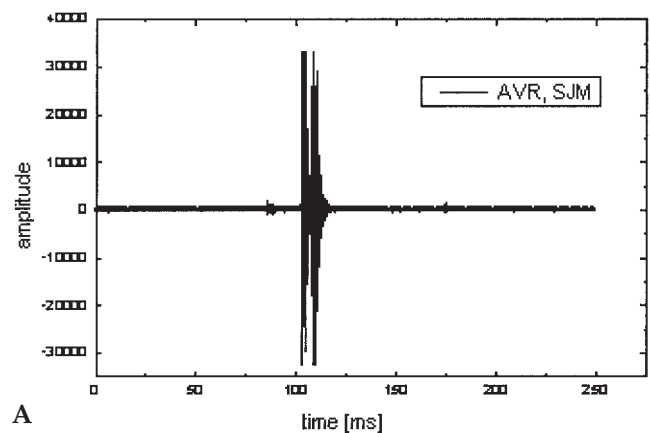


Figure 3: A) Acoustic signal in the patient with undisturbed valve function shows two amplitude maxima representing the closure clicks of both leaflets. B) Acoustic signal with impaired leaflet motion; only one maximum is visible.

ic valve revealed massive thrombus formation at the valve prosthesis. Before and after surgery the valve sounds were recorded with a ThromboCheck. Figure 2A and B illustrate the focal point of frequency and the relationship of the acoustic energy of the two leaflets. Both parameters were changed significantly.

Subsequently, because of another operation, anticoagulation was switched to unfractionated heparin. At five days postoperatively, the ThromboCheck measured a pathological frequency spectrum typical for restricted leaflet motion (Fig. 3A and B). Neither TTE nor TEE revealed any irregularity. X-ray fluoroscopy demonstrated impaired leaflet motion.

#### Case no. 3

This 74-year-old male underwent AVR with a SJM 31-mm composite valve graft, but was admitted to hospital at 38 days postoperatively for bleeding from

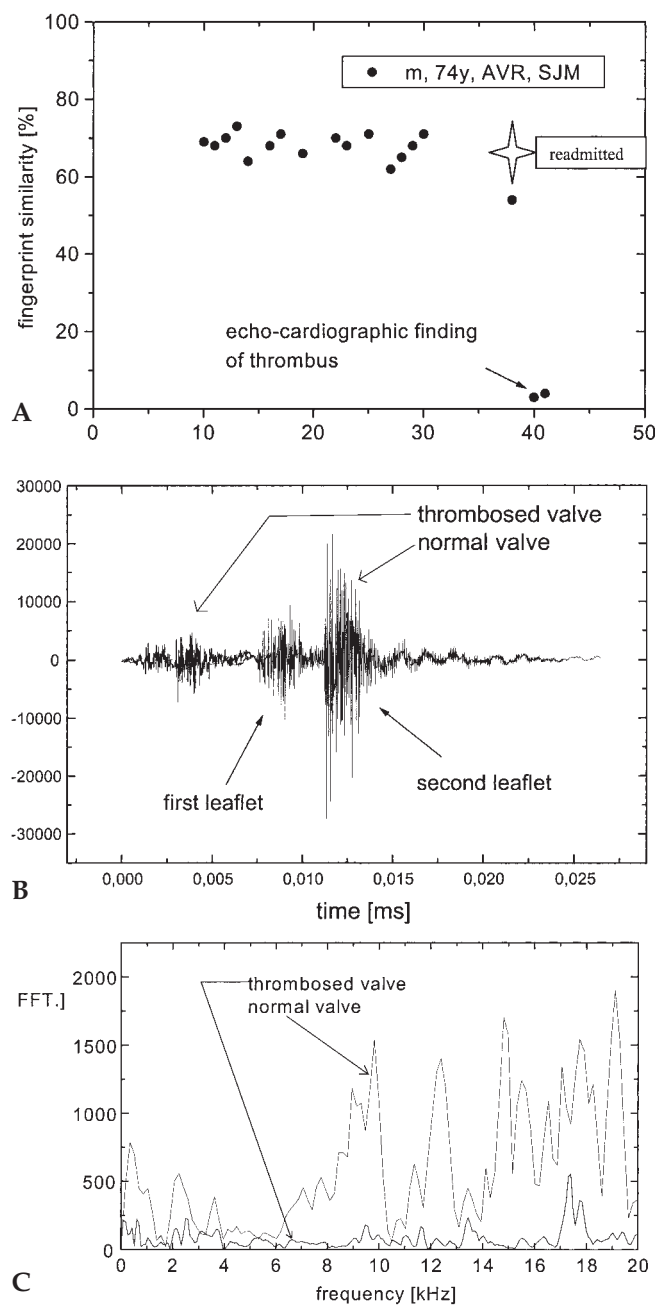


Figure 4: A) The course of ThromboCheck measurements shows a reduction in fingerprint similarity to less than 10%. B) The intact prosthetic valve's frequency spectrum shows a maximum for each leaflet. The thrombosed prosthetic valve's frequency spectrum only shows a 'single-click' because of complete blockage of one leaflet. The amplitude was reduced by factor 30, representing the beginning of thrombus formation at the second leaflet. C) Fast-Fourier transformation (FFT) of the signal shows that certain frequencies are significantly reduced, or could no longer be detected.

esophageal varices due to liver cirrhosis. This patient was monitored with the ThromboCheck once daily. The first signal had already documented changes within the primary frequency spectrum. Invasive hemodynamic monitoring with a Swan-Ganz catheter was inconspicuous. Consecutively performed TEE and angiography revealed complete immobilization of one leaflet, while motion of the other leaflet was regarded as 'normal'. However, the frequency spectrum showed a significant reduction in the amplitude of both leaflets (Fig. 4A-C).

#### Case no. 4

This 64-year-old female underwent AVR with an SJM valve. She was admitted to hospital with suspected prosthetic valve dysfunction; this was diagnosed by TEE, and confirmed by investigation with the ThromboCheck. On reoperation, thrombotic material was found predominantly at the sewing ring (Fig. 5).

## Discussion

Previous investigations in animals and patients have demonstrated that the acoustic sound phenomena of prosthetic heart valves remain constant over time. However, the same prosthetic device, when implanted in various animals and patients, may produce different sound pressures. These differences may be due to individual flow and resonance conditions. Furthermore, it could be demonstrated that each valve replacement device produces characteristic frequency spectra.

Pathological processes involving heart valve prostheses result in distinct changes to the acoustic signals that are characteristic of the respective device. Previous experimental studies have shown that the spectral analysis of click sounds indicated prosthetic valve dysfunction long before echocardiography, fluoroscopy or hemodynamic measurements were suggestive of any disturbed valve function. Thrombolysis does not seem justified if only the frequency analysis shows a pathological result, though the patient should be intensely screened. Thus, a suitable hand-held device for signal recording represents an ideal option for the home monitoring of prosthetic valve integrity.

It should be conceded that the frequency spectrum of prosthetic clicks must be influenced by changes in hemodynamics or atrial fibrillation. A screening method requires high sensitivity but not necessarily high specificity, as differential diagnosis will be made by the cardiologist once the control device has indicated a prosthetic problem.

Fourteen patients of subgroups 1, 2 and 3 were identified by pathological frequency analysis (1.1% in group 1; 10% in group 2; 11% in group 3). Only in one patient in subgroup 3 was the frequency analysis inter-



Figure 5: A thrombosed prosthetic valve (St. Jude Medical); thrombotic material was found predominantly at the sewing ring.

preted as a false negative. However, the subgroups included different patient populations (positive selection regarding age, compliance, INR self-management, etc.). The present results suggest that prosthetic valvular dysfunction without clinically apparent symptoms seems to occur more frequently than is generally presumed. This suggestion is supported by the results of studies dealing with the occurrence of high-intensity transient signals (9).

This observation could be of imminent importance, especially in developing countries where a high percentage of the inhabitants live in rural areas and there are huge distances between medical centers, with consequent long time intervals between INR measurements. The ThromboCheck provides reproducible results of frequency analyses, and is also easy to use. Moreover, prosthetic valve dysfunction is detected early enough to prevent severe, or even fatal, consequences.

Several groups have studied the acoustic signals of Björk-Shiley mechanical valves following strut fracture (10-17), but none of the reports of in-vivo testings has presented individual baseline measurements revealing an individual, fingerprint-like frequency spectrum.

The present authors' studies have contributed to the development of the first hand-held device for home monitoring of heart valve function, and this is currently being tested under clinical conditions.

One potential disadvantage of such a device is an increase in patient concern. However, the results of the questionnaire indicated that patients may feel safer, and that the device may help them to cope with the inevitable disadvantages of a mechanical heart valve. In a recent study, 307 persons aged 50 years or more were interviewed with regard to their attitude to the

application of innovative technology in their private living space and healthcare. They were also asked whether they were prepared to use telemonitoring and smart home care in their personal surroundings. In fact, 96% of the participants supported the idea of using such features and systems, especially for the care and monitoring of chronically ill people. In addition, 83% expected that their desire for more safety would be met, and 73.3% felt that this technology would probably save time and increase the mobility and independence of older patients (70.8%). Only 11.7% suggested that telemonitoring and smart home technologies were unnecessary and would only cause fears (18).

Faced with this background - and considering the fact that whilst home monitoring cannot substitute for regular physician consultation, it might minimize time intervals between investigations and allow early diagnosis of prosthetic valve-associated complications - patients may benefit significantly from devices which offer them greater safety and an improved quality of life.

The efforts aimed at a maximum reduction in INR levels - and therefore at a further reduction in hemorrhage-related complications - seem reasonable. It even seems realistic that in the near future, and under certain conditions, a patient who has undergone heart valve replacement with a mechanical prosthesis can be treated without the use of coumarin derivatives. One of these conditions would be the availability of a tool such as the ThromboCheck, which is able to analyze the frequency spectra of valve sounds. Whether in the future patients bearing mechanical prostheses may be treated solely with aspirin, for example, remains to be seen. However, the pursuit of this path - which would certainly lead to an elimination of hemorrhage-related complications - requires that clotting-related complications are detected immediately and treated when necessary.

### Therapeutic considerations

The incidence of prosthetic heart valve obstruction through non-infectious mass is considered to be 0.5% per year after AVR, and up to 2.5% per year after MVR (19). These values are considerably higher in poorly controlled populations, for example in developing countries. Several studies have indicated the impact of thrombolysis or valve re-replacement on prognosis (20-23). Recently, the present authors presented preliminary results of simulation and animal studies related to the recording and transmission of acoustic sound phenomena (5). Further investigations have concentrated on a reliable implementation of the Doppler probe. If these efforts progress successfully, it could be envisaged that this type of home monitoring will be

made available to a large patient clientele. The present type of device will certainly be important in future for the early detection of relevant dysfunctions in heart valve prostheses, as well as in the observation of medically treated cardiac patients, a reduction in their anti-coagulation, and thereby a reduction in thromboembolic and bleeding complications.

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