

4. Mohammad S., Zhengfeng Z., Qiuming G., January G.T. Blockage of the HERG human cardiac K<sup>+</sup> channel by the gastrointestinal prokinetic agent cisapride. // *Am. J. Physiol.* 273 (Heart Circ. Physiol. 42). 1997. P. H2534-H2538.
5. Wysowski D.K., Bacsanyi J. Cisapride and fatal arrhythmia. // *N.Engl. J. Med.* 1996. V. 335. P. 290-291.

## **НЕЙРОГУМОРАЛЬНІ ЕФЕКТИ МЕТОКЛОПРАМІДУ**

*С.М. Панчук, В.Б. Жукова, І.О. Бондаренко, О.М. Пасько, І.В. Соловійова*  
Харківський національний університет ім. В.Н. Каразіна

---

### **РЕЗЮМЕ**

З використанням технології варіабельності серцевого ритму (ВСР) вивчені нейрогуморальні ефекти метоклопраміду у 18 здорових волонтерів в умовах гострої фармакологічної проби. Установлено, що метоклопрамід знижує загальну потужність нейрогуморальної регуляції (НГР) більшим чином за рахунок пригнічення активності симпатичної та, меншим чином, парасимпатичної складової цієї потужності. Ступінь впливу препарату на показники НГР визначався початковим симпато-вагальним балансом обстежених. Не виявлено впливу метоклопраміду на направленість реакцій показників ВСР в ортостазі. Дія препарату була обмежена більш значним зменшенням вкладу у регуляторні механізми парасимпатичної складової із зсувом вегетативного балансу у напрямку симпатикотонії. Ці зміни не залежали від початкового стану симпато-вагального балансу обстежених. Установлена індивідуальність реакцій нейрогуморальних систем на метоклопрамід потребує його попереднього тестує 66 і у гострій фармакологічній пробі, а оптимальний менеджмент пацієнта вимагає планування дози та с і призначення препарату.

**КЛЮЧОВІ СЛОВА:** нейрогуморальна регуляція, варіабельність серцевого ритму, метоклопрамід

## **THE NEUROHUMORAL EFFECTS OF METOCLOPRAMIDUM**

*S.N. Panchuk, V.B. Zhukova, I.A. Bondarenko, H.N. Pasko, I.V. Solovjova*  
The Karazin National University of Kharkov

---

### **SUMMARY**

Neurohumoral effects of metoclopramidum on 18 healthy volunteers were studied with the help of heart rate variability technology (HRV) under acute pharmacological test conditions. The obtained results indicated that metoclopramidum decreases the total power of neurohumoral regulation (NHR) mostly by depressing sympathetic activity and least - parasympathetic one. The degree of the preparation effect on HRV indexes was determined by the initial sympathovagal balance of the volunteers. Metoclopramidum did not show the ability to modify the directions of HRV parameter changes in conditions of active tilt test. The preparation effect was limited by more significant deposit decrease of a parasympathetic component with a shift of autonomic balance towards sympathetic influences. The above effect was not determined by the initial values of sympathovagal balance. The determined individuality of the neuroregulatory systems response to metoclopramidum intake requires its preliminary testing in acute pharmacological test. The optimal management of a patient requires planning of the dose and regimen of a medication intake.

**KEY WORDS:** neurohumoral regulation, heart rate variability, metoclopramidum

*УДК: 61: 002*

## **INTERNET - BASED TELEMONITORING OF INTRAMYOCARDIAL ELECTROGRAMS**

*H. Hutten*

Institute of Biomedical Engineering Technical University, Graz (Austria)

---

### **SUMMARY**

Purpose of the work: The potential of the Internet for worldwide transmission of intramyocardial electrograms (IMEGs) has been evaluated in order to provide permanent access to centers that are specialized in computerized signal processing.

**Materials and Methods:** In 1992 the project CHARM (Computerized Heart Allograft Recipient Monitoring) has been started for monitoring the rejection in transplanted hearts. IMEGs are acquired by using a pacemaker system with capability for broad-bandwidth telemetry together with fractally coated electrodes in either epimyocardial or intraventricular position. The IMEGs are transmitted to a data acquisition station, where they are stored, analogue-to-digital converted and fed into the Internet after adding some clinically relevant data and encrypting. Internet transmission is mainly performed with the FTP protocol, but in some cases alternatively with e-mail. At the processing center, password secured data account has been installed for each connected hospital. Patient identification is achieved by utilizing the pacemaker identification code that is heading the transmission of the IMEGs to the data acquisition station. After signal processing and parameter extraction, complete patient reports are provided for the sending hospital.

**Results:** Up to now more than 26.000 IMEG sequences each containing about 100 events have been sent to the processing station in Graz from 285 patients and 14 hospitals around the world. No transmission problems or erroneous transmission utilizing standard transmission protocols have been observed. It had been possible in any case to consider appropriately the firewall concept of the hospitals and adjust the transmission procedure to the requirements of the hospital. In the meantime computerized IMEG assessment is used not only for transplant monitoring, but for recipient monitoring and for hemodynamic assessment.

**Conclusion:** Internet-based transmission of IMEGs to specialized centers for computerized signal processing has proven to be reliable and thus renders possible the establishment of cardiac telemonitoring. The center for signal processing can supply additional service for hospitals like data management in multicenter studies.

**KEY WORDS:** intramyocardial electrograms, transplanted heart, Internet, telecommunication technology

## INTRODUCTION

Modern health care systems will be based on extended utilization of advanced digital telecommunication technology that becomes more and more available, e.g. GSM based mobile telephone systems, Internet and comparable medical intranets, satellite-based transmission systems. Worldwide transmission of medical data will render possible different applications of telemedicine, e.g. teleconferencing, teleconsultation, telesurgery, telehomecare. The most popular definition of telemedicine has been proposed already in 1983 by Conrath [2]: „Telemedicine is the use of the telecommunication technology to assist in the delivery of health care.“ Also in 1983, Lerch has emphasized that modern telecommunication promises to solve one of societies most pressing problems: the sharing of a limited number of resources among a large number of users when resources also mean expertise, wisdom and knowledge [6]. Many research projects have been initiated in the last few years, e.g. funded by the European Union [1] and the G8-group to assess the potential of telemedicine/telematics for health care delivery. Special regards have been reliability, availability and costs.

This report here is based on a project that has been started 8 years ago. The aim of this project has been to use advanced pacemaker devices in combination with modern telecommunication technology and data processing systems for rejection monitoring in heart transplant recipients [3]. The challenge has been to assess medical telemonitoring of patients with regard to therapy management, e.g. surveillance of patients with

high cardiovascular risk factors. For the advancement of that methodological approach in the near future it is necessary to develop appropriate forms of organizational structures as well as networks and equipment that can be employed for temporary or permanent monitoring without requiring that the patient has to stay in the hospital. In that project, another attractive possibility for utilizing the worldwide transmission of medical data has also been evaluated, the support of multicenter studies by specialized service institutes. Frequently multicenter studies are based on standardized procedures for signal and data processing that employs tailored software which is not available or usable in all participating clinical centers.

## MATERIALS AND METHODS

The project CHARM (Computerized Heart Allograft Recipient Monitoring) [4] has been evaluated as alternative to endomyocardial biopsy diagnosis in patients after heart transplantation. Intramyocardial electrograms are acquired with fractally coated electrodes either in epimyocardial or right intraventricular position. Electrograms are obtained from the spontaneously beating (spontaneous ventricular events SVE) as well as from the paced heart (Ventricular Evoked Response VER) and transmitted by a dual-chamber pacemaker to an extracorporeal data acquisition device. This short-distance transmission is using broad-bandwidth inductive coupling in order to obtain electrograms with diagnostic quality and resolution (Fig.1). Usually electrogram sequences of 1 minute representing about 80-100 events are considered for a data file.

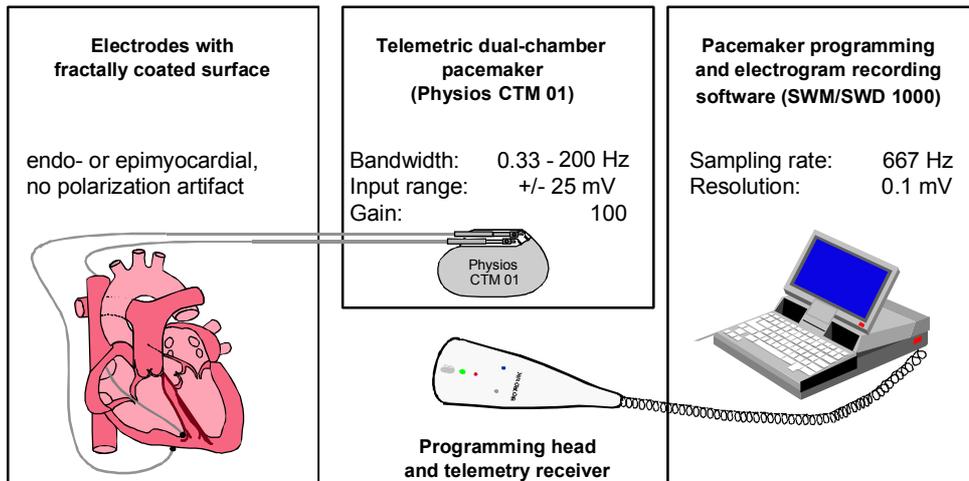


Fig. 1. The IMEG recording system consists of electrodes with fractally coated surface, the telemetric dual-chamber pacemaker and the data acquisition unit

In the data acquisition station the electrogram 68 are analogue-digital converted with a sampling rate of 667 Hz and a resolution of 0,1 mV, supplemented with clinical data as agreed in the study protocol, and related to corresponding patient data. After transferring the data into a transfer file, appropriate data compression and encrypting, the data are transmitted via the Internet to the central data processing and analysis center in Graz (CORTRONIK, <http://www.cortronik.co.at>). All appliances (electrodes, pacemakers, data acquisition station) are available from BIOTRONIK (Berlin, Germany). At the center in Graz data processing and analysis is performed using tailored software. The results of the recent analysis are added to the former patient record

and returned to the sending hospital within few minutes. The schematic structure of CHARM is illustrated in fig. 2. Fig. 3 depicts the flowchart of the operating and data processing tasks as performed in each hospital and in the analysis center. In fig. 4 the electronic form is shown that has been developed to enter patient and examination data in the hospital before transmitting the data file to Graz. This electronic form can be adjusted to the special wishes and requirements of each hospital. Fig. 5 presents a typical patient record as it is returned from Graz to the sending hospital where the receiving station is available. This record can be visualized and printed or stored in electronic form.

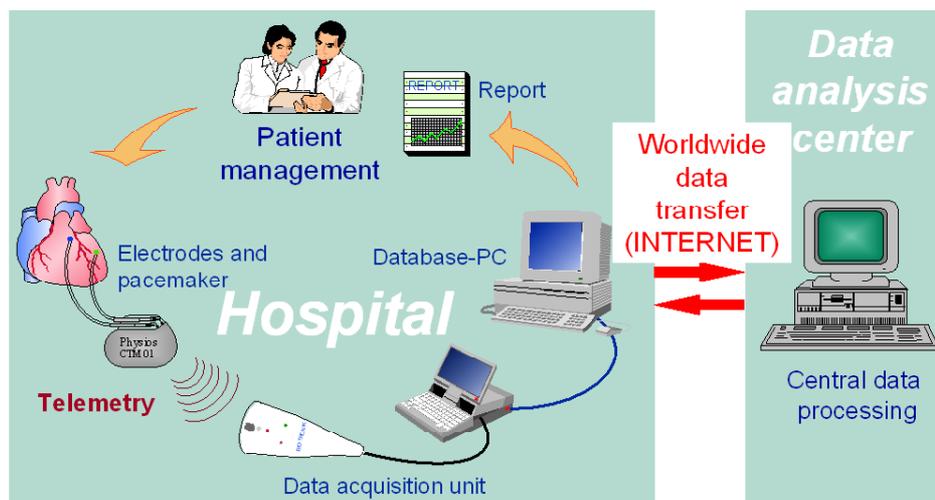


Fig. 2. Schematic structure of CHARM (Computerized Heart Allograft Recipient Monitoring)

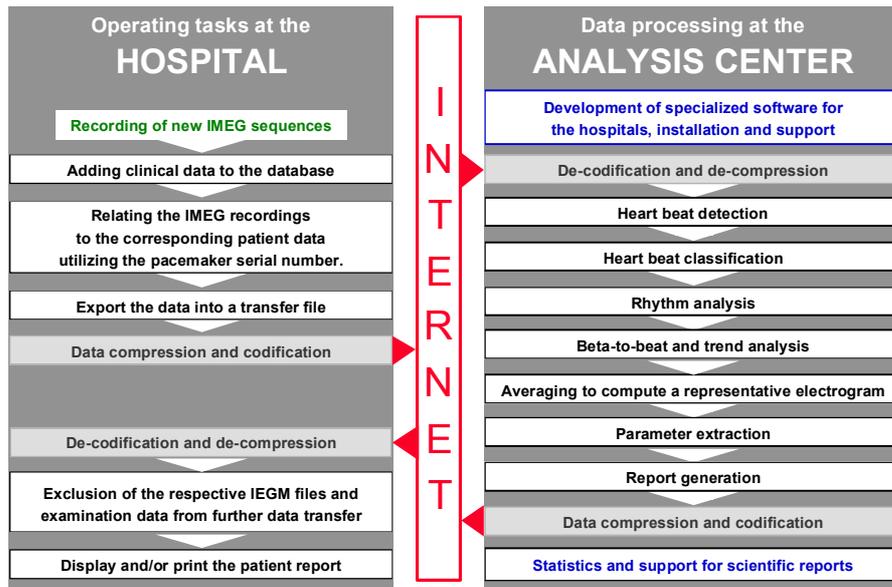


Fig. 3. Flow chart of the operating and data processing tasks as performed in each hospital and at the analysis center

**CHARM**  Search 69 **EXAMINATION**

Patient-ID:  \* Date of examination: 31.03.1999

Status:    
 Weight:  [kg]  
 Body temperature:  [°C]

**Endomyocardial biopsy:** ?   
 Single specimens:  [ISHL 1]

**Basic immunosuppression**

Cyclosporine:  [mg/day] Level:   
 Azathioprine:  [mg/day] WBC:  [G#]  
 Steroides:  [mg/day]  
 Mycophenolate:  [mg/day] Level:   
 FK 506:  [mg/day]

**Rejection therapy** ?

Steroides:  [mg/day]  
 R-ATG:  [mg/day]  
 BT 563:  [mg/day]  
 OKT 3:  [mg/day]  
 FK 506:  [mg/day]

**Infectious disease:** ?   
 Occurance:    
 Pathogen:    
 Therapy:    
 Diagnosis:

**Electrolytes**

Ca:  [mmol/l]  
 K:  [mmol/l]  
 Na:  [mmol/l]

**Catecholamines:**   
**Calcium channel blockers:**   
**Beta blockers:**   
**Other antiarrhythmic drugs:**   
**Lipid lowering agents:**

**Echocardiography**

LVDD:  [mm] RVDD:  [mm]  
 LVSD:  [mm] EF:  [%] RVSD:  [mm]  
 MINS:  [0-4] SF:  [%] TRINS:  [0-4]

**CAUTION!**

Comment:

Fig. 4. Example of an electronic database form

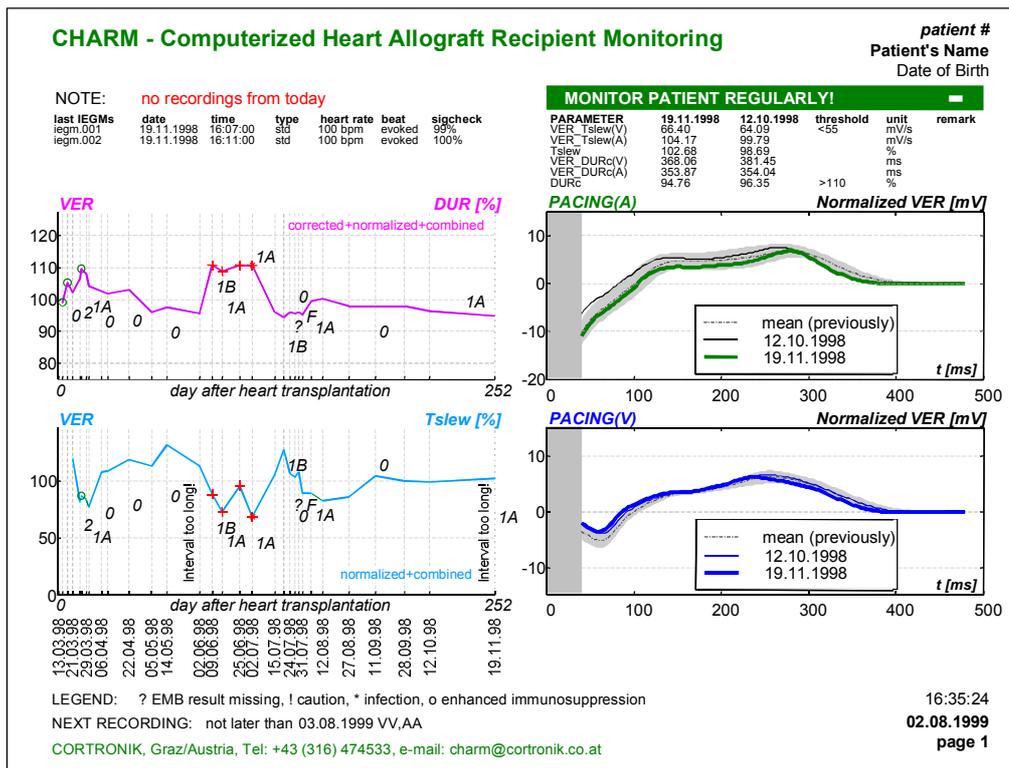


Fig. 5. Example of a regular patient report. On the left hand side trend curves of the diagnostic parameters are displayed relative to prospectively calculated diagnostic thresholds. The right hand side shows current and previous averaged IMEGs from both pacemaker channels. The tables above contain detailed information about the most recent recordings and the parameter values, respectively

Data transmission is performed using the FTI protocol in order to appropriately consider the firewall concept of the hospitals. If the FTP protocol is not available at the participating hospital, data transmission can also be accomplished via e-mail. In Graz a password secured data bank account is installed for every hospital. Each patient is identified by the pacemaker identification code that is heading the transmitted data file. Additional safety measures are considered including special procedures for signal analysis.

### RESULTS AND DISCUSSION

Since the beginning of CHARM, about 26.000 electrogram sequences from 285 patients in 14 hospitals around the world have been transmitted to Graz (fig. 6). No serious or real difficulties have occurred that fundamentally question the suitability and reliability of the Internet for this kind of data transmission. Usually the transmission of the complete data file (about 40 kByte after adequate data compression) to Graz requires only a few seconds if full transmission capacity is

70

available. During short periods of limited availability of the transmission capacity the required time can increase to less than one minute.

In the course of CHARM two multicenter studies have been supported. The first study is already finished whereas the second one is still running. No serious problems have been observed during these studies. There is clear evidence that the clinical partners benefit from the support provided by the center in Graz. This support is of special importance if the hospitals are using different software platforms that must be adjusted to the data acquisition station or the receiving station. The acceptance in the hospitals is excellent. The complete data management is performed by the analysis center. The hospitals do not need software specialists for taking care of the respective multicenter tasks. The operating procedures in the hospitals are organized in such a way that medical doctors with some training can perform all required tasks. Training can be provided by the center in Graz using teletraining.

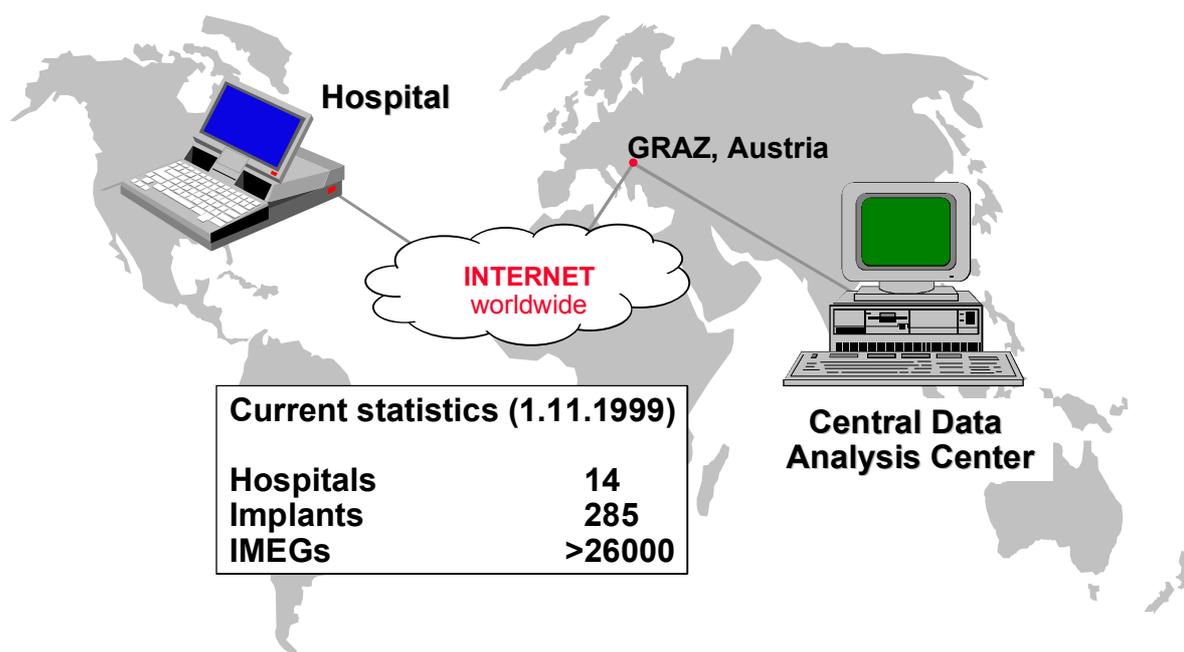


Fig. 6. Current statistics of the cardiac telemonitoring system

In most countries which are either highly industrialized or in the transition phase, the expenses for the health care systems are continuously increasing since many years, as expressed in percent of the national gross domestic product. It is estimated that the current medical insurance system will soon run out of money as a result of spiraling medical costs. This situation is enhanced by the change in the demographic distribution that illustrates the aging problem in most nations. As a consequence of that situation, some countries have already begun to limit or to reduce the services provided by public or general insurances. On the other hand, there is enhanced request for complete and efficient health care as promised in the WHO program 2000. Hence, the demand for a significant modification of the present health care

system is urgent, especially regarding the needs of the elderly people and for chronically ill people with high risk factors. One of the keys to solve those problems may be the utilization of modern telecommunication technology for health care purposes.

In the present study the suitability of the Internet and comparable intranets for cardiac telemonitoring by worldwide transmission of medical data has been proven [5]. It has been shown that pacemakers with telemetric capabilities can be integrated into networks for worldwide data exchange. Although the technical equipment that is required for data acquisition and monitoring is not available for all potential applications, it is now possible to define user requirement documents and technical standards.

## REFERENCES

- Berger R und Partner. Telematikanwendungen im Gesundheitswesen - Perspektiven der Telemedizin in Deutschland. Studie im Auftrag des deutschen Bundesministeriums für Bildung, Wissenschaft und Technologie und des deutschen Bundesministeriums für Gesundheit. 1997.
- Conrath DW. Evaluating telecommunication technology in medicine. Dedham-Massachusetts, Artech House. 1983
- Hutten H et al. Der Herzschrittmacher als Brücke zum kardialen Telemonitoring. // Biomedizinische Technik. 1996. V. 41. P. 158-165.
- Hutten H et al. CHARM - Computerized Heart Acute Rejection Monitoring. // Biomedizinische Technik. 1996. V. 41. (Suppl. 2). P. 35-40.
- Kastner P et al. The cardiac telemonitoring system in clinical practice - preliminary results of a multicenter study. // Medical & Biological Engineering & Computing. 1999. V. 37. (Suppl.2). Part II. P. 1440-1441.
- Lerch IA. Progress in telemedicine. In: Bajzer Z, Baxa P, Franconi C (Eds.): Proceedings of the II. International Conference on Applications of Physics to Medicine and Biology, Singapore, World Scientific Publishing. 1983. P. 435-478.

## ИНТЕРНЕТ - ТЕЛЕМОНИТОРИНГ ИНТРАМИОКАРДИАЛЬНЫХ ЭЛЕКТРОГРАММ

Г. Хуттен

Институт Биомедицинской техники  
Технический Университет Граца (Австрия)

---

### РЕЗЮМЕ

Оцінена можливість мережі інтернет для всевітньої передачі інтраміокардіальних електрограм (ІМЕГ) і забезпечення постійного доступу до центрів, що спеціалізуються в автоматизованій обробці сигналів.

Для моніторингу процесів відторгнення пересаженого серця у 1992 був створений проект CHARM (Автоматизований серцевий алографічний моніторинг реципієнтів), ІМЕГ записувалися з використанням системи кардіостимулятора, що володіє можливостями телеметрії із широкою пропускнуою здатністю і має у своєму складі фракційно обкутані електроди, розташовані в епіміокардіальній чи у внутрішньошлунковій області. ІМЕГ передавалися до місця збору даних, де вони зберігалися, піддавалися аналоговому і цифровому перетворенню і передавалися через інтернет після додавання деяких клінічно значимих даних і шифрування. Передача інформації через мережу інтернет здійснювалася головним чином з використанням FTP (протоколу передачі файлів), але в деяких випадках альтернативно за допомогою електронної пошти. Для захисту обліку запису даних, що надходять з кожної лікарні, у центрі обробки даних був встановлений індивідуальний пароль. Ідентифікація пацієнтів досягалася з використанням пізнавального коду кардіостимулятора, передача якого передувала передачі ІМЕГ. Після обробки сигналів і обчислення різних параметрів складалася звіт по кожному пацієнту, котрі далі направлялися у відповідну лікарню.

Дотепер більш 26.000 записів ІМЕГ від 285 пацієнтів і 14 лікарень в усьому світі, що містять приблизно 100 подій кожна, були послані на станцію обробки в Граце. При цьому не було зафіксовано ні однієї проблеми чи передачі помилкової передачі. Став можливим також розгляд концепції міжмережового захисту окремих лікарень і коректування процедури передачі відповідно вимогам лікарні. Водночас автоматизована оцінка ІМЕГ використовувалася не тільки для контролю трансплантата, але і для контролю реципієнта й оцінки гемодинаміки.

Інтернет-передача ІМЕГ на спеціалізовані центри автоматизованої обробки сигналів є надійним інструментом кардіального телемоніторингу. Центр обробки сигналів може забезпечувати лікарні такою додатковою службою, як обробка даних для багатоцентрових досліджень.

**КЛЮЧОВІ СЛОВА:** інтраміокардіальна електрограма, пересажене серце, Інтернет, телекомунікаційні технології

72

## ИНТЕРНЕТ - ТЕЛЕМОНИТОРИНГ ИНТРАМИОКАРДИАЛЬНЫХ ЭЛЕКТРОГРАММ

Г. Хуттен

Институт Биомедицинской техники  
Технический Университет Граца (Австрия)

---

### РЕЗЮМЕ

Оценена возможность сети интернет для всемирной передачи интрамиокардиальных электрограмм (ИМЭГ) и обеспечения постоянного доступа к центрам, специализирующимся в автоматизированной обработке сигналов.

Для мониторинга процессов отторжения пересаженного сердца в 1992 был создан проект CHARM (Автоматизированный сердечный алографический мониторинг реципиентов), ИМЭГ записывались с использованием системы кардиостимулятора, обладающего возможностями телеметрии с широкой пропускной способностью и имеющего в своем составе фракционно окутанные электроды, расположенные в эпимиокардиальной или во внутривентрикулярной области. ИМЭГ передавались к месту сбора данных, где они сохранялись, подвергались аналоговому и цифровому преобразованию и передавались по интернет после добавления некоторых клинически значимых данных и шифрования. Передача информации через сеть интернет осуществлялась главным образом с использованием FTP (протокола передачи файлов), но в некоторых случаях альтернативно с помощью электронной почты. Для защиты учета записи данных, поступающих из каждой больницы, в центре обработки данных был установлен индивидуальный пароль. Идентификация пациентов достигалась с использованием опознавательного кода кардиостимулятора, передача которого предшествовала передаче ИМЭГ. После обработки сигналов и вычисления различных парамет-

ров, составлялись отчеты по каждому пациенту, которые далее направлялись в соответствующую больницу.

До настоящего времени более 26.000 записей ИМЭГ от 285 пациентов и 14 больниц во всем мире, содержащих приблизительно 100 событий каждая, были посланы на станцию обработки в Граце. При этом не было зафиксировано ни одной проблемы передачи или ошибочной передачи. Стало возможным также рассмотрение концепции межсетевой защиты отдельных больниц и корректировка процедуры передачи соответственно требованиям больницы. В то же время автоматизированная оценка ИМЭГ использовалась не только для контроля трансплантата, но и для контроля реципиента и оценки гемодинамики.

Интернет-передача ИМЭГ на специализированные центры автоматизированной обработки сигналов является надежным инструментом кардиального телемониторинга. Центр обработки сигналов может обеспечивать больницы такой дополнительной службой, как обработка данных для многоцентровых исследований.

**КЛЮЧЕВЫЕ СЛОВА:** интрамиокардиальная электрограмма, пересаженное сердце, Интернет, телекоммуникационные технологии

*УДК 61: 002*

## **MONITORING OF INTRAMYOCARDIAL ELECTROGRAMS AND THEIR DIAGNOSTIC POTENTIAL**

*H. Hutten*

Institute of Biomedical Engineering Technical University, Graz (Austria)

---

### **SUMMARY**

**Purpose of work:** Assessment of the potential of intramyocardial electrograms (IMEGs) for longterm cardiac telemonitoring that is not possible by surface ECG due to the poor reproducibility of these signals.

**Materials and methods:** With the availability of cardiac pacemakers with broad-bandwidth telemetry (0,3-200 Hz) and fractally coated electrodes the monitoring of IMEGs both from the spontaneously beating and the paced heart became possible. These signals have first been utilized to monitor rejection in transplanted hearts. Protocols for standardized clinical examinations have been set up that allow to eliminate errors (e.g. time of day, changes in posture, and stimulation parameters). Tailored software has been developed for signal processing based on event classification, averaging, and parameter extraction. Individual features like anatomy of the heart and respective position of the electrode require that each patient is considered for its own reference.

**Results:** IMEGs can be acquired with excellent long-term reproducibility of signal morphology. In most cases the transitory effects during the post-implant period can appropriately be considered. Regarding reproducibility the IMEGs are superior to surface electrograms. Careful signal processing of the structured morphology of IMEGs supplies information of clinical relevance that can not be obtained from surface electrograms. Ventricular evoked responses (VERs) can be obtained with the same electrode that is used for stimulation. VERs in transplanted hearts do indicate not only acute rejection and infection episodes, but have a high prognostic potential for recipient monitoring. Furthermore, IMEGs monitor information on the hemodynamic situation of the heart, e.g. end-diastolic filling volume, and they can be utilized for AV-setting in patients with cardiomyopathies.

**Conclusion:** Surface electrograms are well established for cardiac routine diagnosis and longterm monitoring, e.g. Holter monitoring. However, thanks to progress in pacemaker technology IMEGs offer another challenging potential for cardiac monitoring including therapy management and risk surveillance that is not accessible with surface electrograms. Computerized evaluation of IMEGs is possible, however requires tailored software that is made available by specialized centers.

**KEY WORDS:** intramyocardial electrograms, long-term, cardiac telemonitoring, signal morphology

### **INTRODUCTION**

Recording of intramyocardial electrograms has long been used routinely in order to diagnose or to localize disturbances of the occurrence of excitations and their spreading over the heart [7]. This invasive procedure is restricted to shortterm monitoring. The intramyocardial electrograms are obtained by leads that are transvenously connecting

the heart with an extracorporeal signal receiving station. Usually the signals are acquired with restricted frequency bandwidth. The basic assumption is that the electrode monitors the near-field excitation process, i.e. the summing action potential of a small volume of tissue around the electrode. Typical electrode positions are near the sinus node, the AV-node, the His bundle and along other parts of the conduction pathways. The