DESIGN OF A REAL-TIME EMERGENCY TELEMEDICINE SYSTEM FOR REMOTE MEDICAL DIAGNOSIS

Nuria N. Castellano[abc*], José A. Gázquez[abc], Rosa M. García[abc], Antonio Gracia-Escudero[cd], Manuel Fernández-Ros[c] and Francisco Manzano-Agugliaro[ab].

nnovas@ual.es, jgazquez@ual.es, rgs768@ual.es, antonio.gracia.sspa@juntadeandalucia.es, mfr460@ual.es, fmanzano@ual.es

[a] *Department Engineering. Universidad de Almeria, Almeria. Spain.*

[b] *BITAL - Research Center on Agricultural and Food Biotechnology. University of Almeria. 04120 Almeria, Spain.*

[c]*Group of Electronics, Communications and Telemedicine Research at the University of Almeria, Almeria, Spain.*

[d]*Haematology Unit Manager Torrecardenas Complex Hospital, Almeria, Spain.*

** Corresponding author (Escuela Superior de Ingenieria. Universidad de Almeria. La Cañada de San Urbano. 04120 Almeria. Spain. Phone: +34 950015686, Fax: +34 950015491, email: nnovas@ual.es)*

ABSTRACT

In routine clinical practice emergency care, it is very difficult to perform diagnostic procedures during ambulance transport. This can lead to a delay in the patient's diagnosis0, consequently, in the patient's treatment until arrival at the hospital. Although this situation does not imply notable risk in the majority of pathologies, in anticoagulated patients, this delay can be fatal. In this study, a system is discussed that would minimise the response time until the medical administration of anti-haemorrhagic or antithrombotic treatments that would mitigate or even eliminate the dramatic consequences of the progression of intracranial haemorrhage. The aim of this study is to design a real-time emergency telemedicine system for remote medical diagnosis and to demonstrate that it is possible to perform haematological tests in an ambulance in terms of an international normalised ratio (INR) using wireless transmission, accurately and in real-time, to the referral hospital. The main and novel component of our system is a hybrid network that enables secure long-distance communication from an ambulance. The results of the tests in the ambulance are such that there were no significant differences between the values obtained from the samples analysed during travel in the ambulance and those analysed in the laboratory. Transmitting this information immediately to the hospital may

involve administering early treatment during the transfer as prescribed by the medical staff that has access to both the data and to the patient's clinical history. In conclusion, the telemedicine system designed for real-time emergencies opens new perspectives for remote medical diagnosis.

Keywords: Telemedicine; Real-time Emergency; Remote Medical Diagnosis; Blood Coagulation; International Normalised Ratio.

Table of acronyms

1.

Acronym	Definition
ADSL	Asymmetric Digital Subscriber Line
AF	Atrial Fibrillation
AVF	Augmented Vector Foot, peripheral leads of the electrocardiogram
AVL	Augmented Vector Left, peripheral leads of the electrocardiogram
AVR	Augmented Vector Right, peripheral leads of the electrocardiogram
BP	Invasive Blood Pressure
DVT	Deep Venous Thrombosis
ECG	ElectroCardioGram
ECGx	x Derivation of the ElectroCardioGram
EDC	Error Detecting Code
FFP	Fresh Frozen Plasma
GPRS	General Packet Radio Service
HCT	Hospital Complex of Torrecardenas
ICT	Information and Communication Technology
ICU	The Intensive Care Unit
INR	International Normalised Ratio. It is referred to as the measuring of prothrombin time in the plasma clot after the addition of the tissue factor
IP	Internet Protocol
ISI	International Sensitivity Index
NBP	Non-invasive Blood Pressure
OAT	Oral Anticoagulant Therapy
PT	Prothrombin Time
RESP	Respiration
RS232	Communications interface with Recommended Standard 232
SCADA	Supervisory Control and Data Acquisition
SPO2	O_2 saturation
SPSS	Statistical Package for the Social Sciences
TCP/IP	Transmission Control Protocol/ Internet Protocol
UAL	University of Almeria
UDP	User Datagram Protocol
VKA	Vitamin K Antagonists
VTE	Venous ThromboEmbolism
WHO	World Health Organization

Introduction

Information and communication technology (ICT) has allowed for technical solutions in many fields with social purposes, such as healthcare, allowing the application of new ideas for improvements in the welfare of consumers (Yu et al., 2010). Telemedicine is an umbrella term that encompasses any medical activity involving an element of distance (Wootton, 2001). In telemedicine, the client is separated from the expert in space (Craig and Patterson, 2005). Telemedicine is changing the classical form of healthcare delivery by providing efficient solutions to an increasing number of new situations (Gómez et al., 1996). The development of sensing systems with low-cost sensors and wireless transmission capabilities provides an economic and versatile system for this area of research. Advances in telecommunication technologies have created new opportunities to provide telemedical care as an adjunct to the medical management of patients (Anker et al., 2011). Telemedicine can be useful when there is adequate monitoring, and the system has a direct impact on the fundamental aspects of patient management (Domingo et al., 2012). One of the earliest recorded uses of ICT in telemedicine was when Einthoven, on 7 February 1906, transmitted electrocardiogram (ECG) tracings over telephone lines (Hjelm and Julius, 2005). Telemedicine potentially holds great promise in facilitating emergency medical practice (Amadi-Obi et al., 2014). However, mobile telemedicine applications need to overcome several problems due to vehicle mobility. In the past, wireless communication technologies limited the quality of telemedicine services. Considerable research has been performed in this regard, and several systems have been tested and implemented; however, in those studies, mainly 2G mobile or a satellite for the transmission of ECG and sometimes images (frames) and audio were used (Kyriacou et al., 2009; Sørensen et al., 2011; Novas et al., 2013). In recent years, the advancement of mobile 3G and 4G has spurred new projects (Liman et al., 2012; Laetitia et al., 2014; Wu et al., 2014), e.g., transmitting video, audio and medical data in real time (Ogedegbe et al., 2012; Bergrath et al., 2012) or transmitting haematological data as INR (Walter et al., 2010; Ebinger et al., 2014).

The transfer of critically ill patients requires good coordination to provide patients with the diagnostic tools and the most appropriate treatment for their conditions. Emergency ambulances have two basic objectives: one objective is to move the patient to a hospital, where the patient can be treated more effectively than in the area of origin, and the other objective is to ensure adequate assistance that involves maintaining the state of the patient in the best possible condition until arrival at the hospital of reference (Noguerol et al., 2010).

Anticoagulation with vitamin K antagonist drugs is indicated and controlled in an increasing number of patients. In fact, the number of anticoagulated patients clearly exceeds 1% of the general population (Navarro et al., 2008; Fang et al., 2010). The cause of the growth experienced in recent years is mainly due to the use of it in atrial fibrillation (AF). The prevalence and benefit of anticoagulant therapy is that disease increases with age (Krishnan, 2005). Although prescribing in venous thromboembolism (VTE) is usually temporary (Agnelli and Becattini, 2005; Nieuwlaat et al., 2008), in most anticoagulated patients diagnosed with AF, it is indicated indefinitely (Fang et al. 2010; Nieuwlaat et al., 2008; Agnelli et al., 2003), usually for life. Therefore, this is an acquired hypocoagulability by factorial deficit, with characteristics of a chronic situation (like a chronic disease).

It is important to note that despite the emergence of new oral anticoagulants, which act as inhibitors to coagulation (not by factor deficit) (Jerry Avorn, 2011; Connolly et al, 2009), their use is still not proven (Uchino and Hernandez, 2012; Van der Werf et al., 2012).

Therefore, this chronic situation, with the risks involved, will have to remain prescribed and controlled, at least for some time. Its control test, which is universally accepted, is the international normalised ratio (INR), measuring the prothrombin time in the plasma clot after the addition of the tissue factor; this test can be performed at present using a number of devices (Berkovsky et al., 2006; Caballero-Villarraso et al., 2011) as Coagucheck XS of Roche (Basel, Switzerland), INRatio of Grifols (Barcelona, Spain) or Protime of IZASA (Barcelona, Spain).

The availability of portable coagulometers capable of measuring the prothrombin time (PT) international normalised ratio (INR) in a drop of capillary blood facilitates the decentralization of monitoring by self-testing. Other studies have been devoted to developing calibration models fulfilling the criteria recommended by the World Health Organization (WHO) for the calibration of INR measuring systems (Tripodi, 2013). PT is the main factor used in the control of oral anticoagulant therapy. For measuring PT, thromboplastin is added to the blood sample to activate coagulation, and it causes a blood clot. The time required for clot formation is measured in seconds and is known as the prothrombin time. The PT ratio of patient-to-normal clotting times is (equation 1):

$$\text{PT - ratio} = \frac{\text{PTpatient}}{\text{PTnormal}} \quad (1)$$

In some countries, blood coagulability is usually expressed in a unit called Quick value. However, the result is not quoted in seconds but as a percentage of the normal value. The coagulation times are evaluated in a diagram: the longer the coagulation times are, the lower the percentages are. For a person who does not take any oral anticoagulants (vitamin K antagonists, VKA), the Quick value commonly lies between 70 % and 100 %. A Quick value of 30 % indicates the prolonged coagulation time. The lower the Quick value is, the longer the blood takes to coagulate.

Quick values measured with different thromboplastins are not directly comparable with each other because they for can have different sensitivities to coagulation factors. To make coagulation times comparable, in 1983, WHO adopted a standard reference thromboplastin. WHO recommended using INR instead of Quick value as an indication of the coagulation determination. All manufacturers of thromboplastin must calibrate its reactive in accordance with the WHO standard (there are two references: one for human recombinant thromboplastin and one for rabbit brain thromboplastin). The value obtained is known as the international sensitivity index (ISI). This allows us to determine the different sensitivities of the thromboplastin and this is used to calculate the INR. INR can be calculated according to Equation 2:

$$INR = \left(\frac{PTpatient}{PTnormal} \right)^{ISI} \quad (2)$$

where the ISI is used for testing and represents its responsiveness to the PT prolongation mediated by vitamin K antagonists (Van den Besselaar et al., 1999). WHO recommends that the ISI is less than 1.7. In many countries, an ISI low (1.0) is preferred.

For example, the prothrombin time of a patient receiving oral anticoagulant therapy is 64 s (18 % Quick), and the prothrombin time of a normal plasma is 22 s (100 % Quick). The ISI of the thromboplastin used is 0.93. By substituting this value in equation 2 given above, INR is 2.7. This means that the clotting time is 2.7 times longer than the standard. The longer the clotting time of the patient is, the higher the INR is. The normal value of INR is close to 1.0 for a non-anticoagulated patient. The required level of anticoagulation in patients treated with vitamin K antagonist depends on thromboembolic disease. The most common cases are:

- In patients with atrial fibrillation, the value of INR should be between 2 and 3 permanently and for all life.
- For deep venous thrombosis (DVT), typically, the value of INR should be between 2 and 3 for approximately 6 to 12 months.
- For patients with mechanical valve prostheses, the INR should be between 2.5 and 3.5 (or between 2.5 and 4 if they have other risk factors) permanently and for all life.

Therefore, we continue to face a difficult situation with a narrow therapeutic margin and a high tendency to lose the required interval (INR out of range).

Additionally, we continue to face a difficult situation with a narrow therapeutic margin and a high tendency to lose the required interval (INR out of range). This feature is due to extremely frequent interactions of VKA with other medications and its variability with changes in dietary habits (Molina et al., 2006). Thus, given the relative ease of misuse and the high risk involved, frequent monitoring is required (Molina et al., 2006; Ansell et al., 2008). For this purpose, more accessible systems have been developed, such as digital puncture and processing by small coagulometers for determining INR with great simplicity and speed (Berkovsky et al., 2006; Bauman et al., 2008). These new portable systems ensure more control for the patient; this can be performed in the clinic or even in the household and be controlled by the medical staff (Bauman et al., 2008). Moreover, thanks to the development of these technologies, a new advantage presents itself because it is self-controlled by the patient (McCahon et al., 2011). This prevents or at least minimises continuous and periodic puncture that eventually depletes vascular access for patients (Gardiner et al., 2005). Thus, there has been a genuine change in INR control procedure, which in turn has led to a significant change in healthcare that was traditionally centralised in hospitals and is currently shifting its primary attention (Caballero-Villarraso et al., 2011; Molina et al., 2006). Conversely, the new model-based monitoring telemedicine system with portable INR meters as the INRatio of Grifols (Barcelona, Spain) or CoaguChekXS of Roche (Basel, Switzerland) both require only a fingerstick for self-test by the patient or the staff responsible for patient care (Ansell et al., 2008; Gardiner et al., 2005). These instruments use disposables strips of measure, which also serve as system instrument calibration. The measurement range is from 0.7 to 7.5 in the INRatio and from 0.8 to 8 in CoaguChekXS. Other portable coagulometers require additional systems to calibrate measure such as ProTime of IZASA (Barcelona, Spain) or CoaguChek S of Roche (Basel, Switzerland). The key recommendations that these monitors must meet for their implementation and performance in self-control and in patients treated with vitamin K antagonists are given in ISO 17593: 2007 (Clinical laboratory testing and in vitro medical devices - Requirements for in vitro monitoring systems for self-testing of oral anticoagulant therapy), and it is completed for use with ISO 22870: 2006 (Point-of Care Testing [POCT] - requirements for quality and competence).

The transfer of critically ill patients, such as those with traumatic brain injury, with the frequent altered state of consciousness that this injury entails, can hinder knowledge regarding the pre-treatment of patients. This is especially difficult in those patients treated with VKA, which increases the probability of bleeding if not treated early, and can increase the severity of the complications presented to the patient. Therefore, knowledge of the hypocoagulability situation of a patient must be obtained with the least possible delay, either by accessing patient records electronically or by determining INR in a bloodless manner (such as digital puncture). Although we currently have sufficient technology to make an INR test on an outpatient basis, even a regular ambulance transmitting the data to the hospital presents more difficulty, and only previous attempts have been made with some parameters such as electrocardiogram and pulse (Gázquez et al., 2006). Therefore, because we lack a suitable transmission system, performing a coagulation test in medicalised ambulances, even if effective, was not efficient.

In this paper, a telemetry system integrating various technologies to establish direct, continuous and permanent contact from the means of transport (ambulance) to the intensive care unit (ICU) of the receiving hospital or other receiving centres is developed, taking the measured data to make a proper and thorough assessment of the patient at each instant. With the intention of advancement to the extent possible, which in our view is a remarkably improved situation in the context of emergency care, our group studies the advantages it could provide an autoanalyser, including portable INR, and a telemetry system for biomedical data in an ambulance. Our intention was to perform the INR test during patient transport and to transfer the data to the referral hospital. With this new and innovative strategy, unlike conventional ambulance transfer, the emergency worker can proceed to two types of innovative care. On the one hand, after the examination of the data transmitted to the hospital by the attending physician, the hospital's doctor may prescribe a treatment that nurses can then administer in the ambulance. On the other hand, given that there are hospital records of the immediate arrival of a medical emergency and their coagulation parameters, medical professionals can anticipate, to the extent possible, assistance by preparing medication or the appropriate blood products, usually fresh frozen plasma (FFP).

Telemetry systems have been incorporated into ambulance operations since 2008, initially transmitting parameters from medical monitors, such as electrocardiogram (ECG), O2 saturation (SPO2) and heart rate, among others. After a haematology autoanalyser was attached (Castellano et al., 2012), we have incorporated a portable INR autoanalyser in the ambulance (Caballero-Villarraso et al., 2011) with the medical monitor. The aim of this work is to describe a telemetry data autoanalyser INR system in the ambulance and the feasibility study in the early treatment of patients with anticoagulant therapy or in suspected cases (in cases of disoriented or unconscious patients). Data transmission uses a system called Network-Internet Radio-Modem Hybrid, which was combined the patents of different communications technologies (Gázquez et al., 2006; Novas et al., 2004).

For the development of this system, the city of Almeria (South of Spain), Hospital Complex of Torrecardenas (part of the Andalusian Public Health Service) and other receptor sites including the University of Almería and University of Málaga (over 200 Km to Hospital Complex of Torrecardenas) have been used as the main stage. The telemetry network has worked properly and uninterruptedly since 2008 to post useful comments from which researchers may draw meaningful conclusions. As for technical issues, the results have shown the stability and robustness of the system.

2. Material and methods

A portable system was designed that allows for the telemonitoring of a patient during the ambulance transfer coordinated by a referral hospital. Unlike most teleambulance applications referenced in previous section that had two modules (Mobile Unit and Central Unit), our system has three modules: (a) The mobile unit (ambulance), where expert assistance is required, (b) repeating units relaying information received from the mobile unit to the receptor sites and (c) receiving units where experts coordinate the transfer and the patient is diagnosed with a user-friendly interface (interactive presentation of information collected by the ambulance), allowing a recording in a digital format with links to healthcare databases to obtain additional information from the patient (Fig. 1).

2.1. Communication system: Red Hybrid Radio-Modem-Internet

This network allows the transmission of biomedical data from the ambulance and a reference hospital with a line-of-sight distance of over 25 km. In addition to the transmitter device and the receiver device, the Hybrid network has a set of relay-based narrowband radio modems, creating an interface between the wireless network and the Internet (ADSL, fibre optics, mobile phones). The radio modems allow for a great scope-power ratio at the expense of a low transmission rate. Thus, this system combines the reach of a radio modem with the widespread use of the Internet, which has an easy to expand infrastructure and very low transmission costs (only data transmitted by mobile phone) (see Fig. 1).

Mobile Unit

The mobile unit is located in an ambulance and consists of a microcontroller with embedded Ethernet and one RS232, which is a serial interface for a narrowband radio modem (set at a speed of 19,200 bits / s and a power of 100 mW for conducting the tests), a medical monitor, an autoanalyser of INR (INRatio2 of Grifols, made in San Jose CA95134 USA), which has an International Sensitivity Index (ISI) close to one with an RS232 interface and a power supply unit supplied from the mains or battery (sealed lead acid, 12 Volt, 7 Amp/h) and a high-efficiency switching regulator (0.8) to provide a stabilised voltage range for several hours.

This unit has the function of extracting the autoanalyser INR information, formatting it, encrypting it and transmitting it through a radio modem (Fig. 2). To comply with the rules of confidentiality, we encrypt the information in real time (Novas et al., 2004). The mobile unit is also equipped with a GPRS modem to fill coverage gaps in the network of own repeaters (hybrid network repeaters) and the accessible telephony network. The system operates autonomously. As soon as the device is turned on, it sends the updated information to the authorised receiver units. Fig. 2 shows the functional diagram for transmitting data from the mobile unit. Fig. 3 shows the basic equipment that makes up the mobile unit.

Own network of repeaters

A repeater is a unit for receiving radio signals transmitted by narrowband mobile units and for forwarding by an embedded processing Internet unit for receiving the stations authorised. The number and strategic locations of the repeaters determine the coverage area of the network. Given the characteristics of the transmission, a large number of repeaters are not necessary to cover a city and peri-urban areas.

The embedded unit is built similarly to the mobile unit, with a difference in the store software. Data radio modem transmissions are received through the RS232 interface and are analysed. After determining that the packet is sent via the Ethernet interface to the IP addresses of the receiving station, this interface may use various protocols such as TCP/IP, UDP, AppleTalk or others (Fig. 4). The destination of the packet is an updatable record that contains the IP addresses of the active reception units (operation) of all IP authorised. It also has other ancillary functions for the remote configuration and management quality of communications, such as enabling or disabling the repeaters, updating the list of receiving units, and reading the statistics of lost packets or the wrong checksum.

Receiving centres

The receiver units are located in the medical centres, where experts monitor the transfer or at any other location from which an expert needs to receive data. They are the ultimate units that receive the information, basically consisting of a computer connected to the Internet and / or corporate network access to databases with information on the medical history of patients and Supervisory Control And Data Acquisition (SCADA) for interactive presentation and evaluation by the medical staff, who can review the medical history to complete the diagnosis (Fig. 5). The decryption system requires prior information and checking the received packet. The data source is marked with a temporary base when generated for proper presentation. The system represents the first packet of information with a valid timestamp, discarding all packets with equal or prior timestamp to and displayed in the interactive application. The application allows the storage and subsequent reproduction of the information.

The communication protocol is implemented using TCP/IP. It has the following functions: informing repeater units of the activity, if the computer was off before running the application and receiving via the Ethernet the information generated in mobile units bound for the receiver unit. In Fig. 6, the flow diagram of the receiving unit is presented. The application represents in real-time the information transmitted (INR level) as patient identification data, alarms and communications statistics to study link status instantly and globally averaged or in a repeater.

2.2. Infrastructure

To validate the proposed system, we established the premise of providing care coverage within 25 Km around the referral hospital, Hospital Complex Torrecardenas (HCT) in Almeria. We distribute four repeaters installed in strategic locations and three receptor sites in the Torrecardenas Hospital, the University of Almería (UAL) and the University of Malaga and a mobile unit.

2.3. Information transmitted

A single type of data packet, which has been treated and prepared for circulating in a safe and optimised manner over the entire system, circulates through the hybrid network. Figure 7 shows the general structure of the packet.

This packet transmits a large amount of different data (Fig. 7), such as the biomedical data provided by the medical monitor (Electrocardiogram (ECG), invasive blood pressure (BP) and non-invasive blood pressure (NBP), O2 saturation (SPO2), pulse, heart rate, respiration (RESP)), INR data and data regarding signal quality and alarms. From this information, a selection is made so that the transmitted data are absolutely necessary to provide an adequate representation of signals to the referral hospital.

The information to be transmitted (packet) mainly has two parts. Part one, the header, is the part that identifies each packet, including the sequence number to sort later, patient data, the date and time. Part two, in contrast, includes the packet body containing the data from the INR tests. The measurement system of the INR tests has been included in the telemetry network where the data captured by the medical monitor were recorded. The original transmitted packet is optimised for transmission over the hybrid network (Fig. 6); therefore, adding new data to the packet without damaging the transmission is a problem. The solution was to design a fixed packet size with variable data fields. This alternative maintains the original packet so that they are constantly sending data captured from the medical monitor until the time that the blood coagulation analyser sends data. At this time, a routine in the hardware interface that involves making a change in the packet header starts, and it will stop sending data that are not critical. In this field of haematological data, a mark is included that acknowledges receiving the application, indicating that the coagulation data are in this packet (see Fig. 7).

The main advantage of this option is that the modifications made to the system are minimal. Perhaps the encapsulation and delivery of data are responsible for the hardware interface being larger.

Figure 8 shows details of the transmitted packet by using the measurement device INR. The measuring information from the INR device is obtained on request. This is performed by transmitting a stream of data that includes the last two bytes of the packet’s error detecting code (EDC), which is a code that checks the integrity of the information of the INR. Our device does not have a system that allows a warning if there is a new test sample, so we will temporarily make requests to check for any new samples to send in memory. To enhance security in the transmission of blood clotting data, these data will be transmitted repeatedly over time to avoid possible losses from default coverage or packet corruption. This process will only take place with the last sample transmitted.

2.4. Verification system with analyser INR

The evaluation of the measurement system took place over a period of three months: two months for static tests and one month for dynamic tests. During processing, biomedical data that are recorded by the medical monitors connected to a partner or a patient simulator are transmitted, even though in this paper, only coagulation parameters are evaluated. Static tests consist of the analysis of 120 blood samples at a rate of three samples per day with healthy volunteers. The mobile unit is in the UAL and analyses samples that arrive at the receiving centre (Hospital Complex of Torrecardenas).

For the dynamic tests, the collaboration of the Andalusian Health Service is needed by equipping one of their ambulances with a mobile unit. We conducted 24 tests for each of the three transferee’s samples, commuting each person over eight transfers to the University of Almería-Hospital Complex Torrecardenas (UAL-HCT). These transfers were performed at different times. In addition, tests on the mobile unit are repeated in the laboratory, with the same volunteers to check the similarity of results. The samples were taken from 19 healthy volunteers and five volunteers who had treatment with Oral Anticoagulant Therapy (OAT). For a statistical evaluation of the data, the software package "Statistical Package for the Social Sciences" (SPSS) version 14 is used for calculating the mean, standard deviation and standard error.

3. Results

In the static INR test in the UAL (research group laboratory), of the 120 samples analysed, all of the results are received in HCT, and the replies were analysed in the Hospital Complex of Torrecardenas. The average time for receiving was 13.2 s, with a standard deviation of ± 0.2 s. In this first phase, the main goal is correct and efficient reception.

In the dynamic tests, 24 results were read and transmitted from the ambulance by the autoanalyser, medicalised INR. The average time for reception was 13.97 s with a standard deviation of ± 0.22 s. As explained above, the INR test was performed on the same patients in the laboratory of HCT. The results are reflected in Table 1. The mean of the 24 INR determinations was 1.09 for patients without OAT and 2.45 for the five patients with OAT. Although some differences could reach statistical significance (due to the low variance by high repeatability of the test), they are not clinically significant, where we obtained an average of 1.06 in untreated patients and 2.38 in patients with OAT. The difference between the measures, as shown in the table above, does not exceed two times the standard error (0.2); therefore, the differences are not statistically significant, with a value of $p < 0.05$. Therefore, we can conclude that there is no difference between the INR test during transport or when conducted at the laboratory.

The communication quality can be defined as the ratio of the number of well received radio packets (avoiding bad checksum or not received) to the total transmitted radio packets. The essential quality of radio communication has two meanings: for graph information because an electrocardiogram of 60 % is needed and for numerical information that has lowest necessities of approximately 1 %. As an example, with this 1 %, numerical information can arrive once with a 15-s delay.

For effective evaluation of communication quality, one route between UAL and HCT was travelled eight times. The communication information for each route travelled was registered, and an average of the whole travel time was calculated. Fig. 9 shows the average of quality communication for each travel time (point as triangle) and the average of all travel times (horizontal line). As shown in Fig. 9, the communication quality is above 73 % for the dynamic test of the ambulance. Because the INR is numerical information, the results are very good.

4. Discussion

Moreover, in the circumstances described above, the clinical status does not always allow the patient to know or refer to his/her medical history. Given this situation, if the patient has any symptoms that may be altered during coagulation pharmacologically VKA (Sintrom, etc.) and if the serious consequences that can occur from this situation are known, the INR test is justified. This determination along with other biochemical parameters will be of great interest to establish an assessment of the risk of bleeding and the haemodynamic status. A serious drawback in the care of patients transferred is the delay in coagulation assays. Until the patient reaches the hospital, caregivers will not perform this test. The time delay in receiving this result and the establishment of a treatment can be fatal.

We chose a portable capillary INR autoanalyser because performing venepuncture in a moving ambulance to sample the patient with the OAT can cause bruising and bleeding. Instead, the determination of the INR in the blood greatly facilitates the process because to take the sample, only a small puncture in the finger (McCahon et al., 2011) is needed. As for the reliability of the device, many studies and reports recommend the patient’s self-use of portable coagulometers in primary care because they exhibit robustness and accuracy by using appropriate computer applications (Salvador et al., 2011; Gardiner et al., 2005). Moreover, the results presented here did not differ significantly from the samples analysed in a laboratory, which is consistent with other studies (Kyriacou et al., 2009; Novas et al., 2013; Noguerol et al., 2010). At the end of the experiment, all physicians involved felt that the system responded with a high degree of quality to the requirements for the medical assessment of the patient from the receiving centre.

5. Conclusions

The real-time emergency system for telemedicine designed for INR remote medical diagnosis has been implemented in an ambulance. The system has been evaluated successfully in different types of tests for static tests, dynamic tests and communication quality. The static test shows that the verification of a biomedical telemonitoring system and the INR autoanalyser worked properly with 100 % reproducibility for INR data. The dynamic test shows that samples analysed in a moving ambulance and samples analysed in the laboratory with which the specialist can prescribe treatment safely do not exhibit statistically significant differences. Data from the INR autoanalyser may reach a specialist in real time to establish a diagnosis and a treatment based on the received data and the clinical history of the patient to begin early treatment during transport, thus avoiding the possible extension of bleeding. The real-time telemedicine system pilot has been implemented, tested and evaluated within the Research Project From 2009-2014 BRANCHES (Meshed Networks Architecture for Applications Sociosanitary). The results verify the interest in the designed system as a new service for real-time emergencies. This study has highlighted implications for future telemedicine systems by evaluating the effectiveness of the real-time emergency system.

Acknowledgements

This paper was supported by the Spanish Ministerio de Ciencia e Innovacion under grant TEC2009-13763-C02-02 and FEDER. The authors also received support from the Research Group Plan Andaluz de Investigacion TIC019. The telemetry system used in this work was developed as a part of this project. Furthermore, we have received assistance from the Almeria Torrecardenas Hospital by using part of their infrastructure for the location of the signal reception equipment and for the installation of antennas, repeater systems and biomedical measurement equipment.

6. References

Agnelli, G and Becattini, C (2005). Long-term therapy of pulmonary embolism. *Ital Heart J*, 6(10), 824-829.

Agnelli, G, Prandoni, P, Becattini, C, Silingardi, M, Taliani, MR, Miccio, M, Imberti, D, Poggio, R, Ageno, W, Pogliani, E, Porro, F and Zonzin, P (2003). Extended oral anticoagulant therapy after a first episode of pulmonary embolism. *Ann Intern Med*, 139(1), 19-25.

Amadi-Obi, A, Gilligan, P, Owens, N and O'Donnell, C (2014). Telemedicine in pre-hospital care: a review of telemedicine applications in the pre-hospital environment. *International Journal of Emergency Medicine*, 7(1), 1-11.

Anker, SD, Koehler, F and Abraham, WT (2011). Telemedicine and remote management of patients with heart failure. *The Lancet*, 378(9792), 731-739.

Ansell, J, Hirsh, J Poller, L, Hylek, E, Jacobson, A, Crowther, M and Palareti, G (2008). Pharmacology and management of the vitamin K antagonists: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th Edition). *Chest*, 133(6 Suppl), 160S-198S.

Bauman, ME, Black, KL, Massicotte, MP, Bauman, ML, Howlett-Clyne, S, Cembrowski, GS and Bajzar, L (2008). Accuracy of the CoaguChek XS for point-of-care international normalized ratio (INR) measurement in children requiring warfarina. *Tromb Haemost*, 99(6), 1097-1103.

Bergrath, S, Reich, A, Rossaint, R, Rörtgen, D, Gerber, J, Fischermann, H, Beckers, SK, Brokmann, JC, Schulz, JB, Leber, C, Fitzner, C and Skorning, M (2012). Feasibility of prehospital teleconsultation in acute stroke - a pilot study in clinical routine. *PLoS ONE*, 7(5), art. no. e36796.

Berkovsky, A, Sergeeva, EV, Suvorov, AV, Uljavova, IS, Kachalova, ND, Klimovich, LG, Samsonova, NN and Kozlov, AA (2006). A modified method of prothrombin time/international normalised ratio determination in capillary blood and monitoring oral anticoagulant therapy. *Clinical Chemistry and Laboratory Medicine*, 44(10), 1214-1217.

Caballero-Villarraso, J, Villegas-Portero, R and Rodríguez-Cantalejo, F (2011). Dispositivos de coagulometría en el seguimiento y control ambulatorio de la terapia anticoagulante oral: Revisión sistemática. *Atención Primaria*, 43(3), 148-56.

Castellano, NN, Gázquez, JA, López, JF and Manzano-Agugliaro, F (2012). Telemetry system for transmission data from an ambulance. *Dyna*, 79(175), 43-51.

Connolly, SJ, Ezekowitz, MD, Yusuf, S, Eikelboom, J, Oldgren, J, Parekh, A, Pogue, J, Reilly, PA, Themeles, E, Varrone, J, Wang, S, Alings, M, Xavier, D, Zhu, J, Diaz, R, Lewis, BS, Darius, H, Diener, H, Joyner, CD and Wallentin, L (2009). Dabigatran versus Warfarin in Patients with Atrial Fibrilatión. *N Engl J Med*, 361(12), 1139-1151.

Craig, J, Patterson, V (2005). Introduction to the practice of telemedicine. *J Telemed Telecare*, 11(1), 3–9.

Domingo, M, Lupón, J, González, B, Crespo, E, López, R, Ramos, A, Urrutia, A, Pera, G, Verdú, JM and Bayes-Genis, A (2012). Evaluation of a telemedicine system for heart failure patients: feasibility, acceptance rate, satisfaction and changes in patient behavior: results from the CARME (CAtalan Remote Management Evaluation) study. *European journal of cardiovascular nursing: journal of the Working Group on Cardiovascular Nursing of the European Society of Cardiology*, 11 (4), 410-418.

Ebinger, M, Winter, B, Wendt, M, Weber, JE, Waldschmidt, C, Rozanski, M, Kunz, A, Koch, P, Kellner, PA, Gierhake, D, Villringer, JB, Grittner, U, Hartmann, A, Mackert, B-M, Endres, M and Audebert, HJ (2014). Effect of the use of ambulance-based thrombolysis on time to thrombolysis in acute ischemic stroke: A randomized clinical trial. *JAMA - Journal of the American Medical Association*, 311(16), 1622-1631.

Fang, MC, Go, AS, Chang ,Y, Borowsky, LH, Pomernacki, NK, Udaltsova, N and Singer, DE (2010). Warfarine discontinuation after starting warfarina por atrialfibrillation. *Circ Cardiovasc Qual Outcomes*, Nov, 3(6), 624-631.

Gardiner, C, Williams, K, Mackie, IJ, Machin, SJ and Cohen, H (2005). Patient self-testing is a reliable and acceptable alternative to laboratory INR monitoring. *Br. J. Haematol*, 128(2), 242-247.

Gázquez, JA, Novas, N, Noguerol, M, Lorente, M and Berenguel, M (2006). Sistema y método de transmisión de datos entre una unidad móvil y una unidad receptora. *ES patente* 2,253,080. 2006 mayo 16.

Gómez, EJ, del Pozo, F, Quiles, JA, Arredondo, MT, Rahms, H, Sanz, M and Cano, P (1996). A telemedicine system for remote cooperative medical imaging diagnosis. *Computer Methods and Programs in Biomedicine*, 49(1), 37-48.

Hjelm, NM and Julius, HW (2005). Centenary of tele-electrocardiography and telephonocardiography. *J Telemed Telecare*, 11(7), 336–338.

ISO 17593:2007. Clinical laboratory testing and in vitro medical devices -- Requirements for in vitro monitoring systems for self-testing of oral anticoagulant therapy. ISO/TC 212. Reviewed in 2011.

ISO 22870:2006. Point-of-care testing (POCT) -- Requirements for quality and competence. ISO/TC 212.

Jerry Avorn, MD (2011). The Relative Cost-Effectiveness of Anticoagulants. Obvious, Except for de Cost and the Effectiveness. *Circulation*, 123, 2519-2521.

Krishnan, K (2005). Atrial fibrillation: management for the geriatric patient. *Am J Geriatr Cardiol*, 14(5), 242-7, quiz 248-9.

Kyriacou, EC, Pattichis, CS and Pattichis, MS (2009). An Overview of Recent Health Care Support Systems for eEmergency and mHhealth Applications. *Proceedings of the 31st Annual International Conference of the IEEE*

Engineering in Medicine and Biology Society, Sep 2-6; Minneapolis, Minnesota, USA, 1246-1249.

Laetitia, Y, Van Hooff, R-J, De Smedt, A, Alexis, VE, Van Rita, D, De Rohny, VC, Andre, C, Ives, H, Door, L, De Jacques, K and Raf, B (2014). Feasibility of ambulance-based telemedicine (fact) study: Safety, feasibility and reliability of third generation ambulance telemedicine. *PLoS ONE*, 9(10), art. no. e110043.

Liman, TG, Winter, B, Waldschmidt, C, Zerbe, N, Hufnagl, P, Audebert, HJ and Endres, M (2012). Telestroke ambulances in prehospital stroke management: concept and pilot feasibility study. *Stroke*, 43, 2086–2090.

McCahon, D, Murray, ET, Murray, K, Holder, RL and Fitzmaurice, DA (2011). Does self-management of oral anticoagulation therapy improve quality of life and anxiety?. *Family Practice*, 28(2), 134-140.

Molina, MP, Sánchez-Garrido, R, Rodríguez, MI, Martínez, JL and Escobar, JL (2006). Control del tratamiento anticoagulante oral en atención primaria de la provincia de Málaga. *Rev. Calidad Asistencial*, 21(6), 293-298.

Navarro, JL, César, JM, Fernández, MA, Fontcuberta, J, Reverter, J and Gol-Freixas, J (2008). Tratamiento anticoagulante oral. Estudio coste/beneficio. *Revista de Administración Sanitaria*, 6(3), 525-42.

Nieuwlaat, R, Dinh, T, Olsson, SB, Camm, AJ, Capucci, A, Tieleman, RG, Lip, GY and Crijns, HJ (2008). Should we abandon the common practice of withholding oral anticoagulation in paroxysmal atrial fibrillation. *Eur Heart J*, 29(7), 915-922.

Noguerol, M, Novas, N, Gázquez, JA, Gil, B, Quintana, M and Heredia, H (2010). Sistema de Telemetría en ambulancia. *Rev. Clínica Española*, 210(supl), 398-399.

Novas, N, Gázquez, JA, and Noguerol, M (2013). Real-Time Biomedical Telemetry System for Ambulances. In M. Cruz-Cunha, I. Miranda, & P. Gonçalves (Eds.) *Handbook of Research on ICTs and Management Systems for Improving Efficiency in Healthcare and Social Care* (pp. 356-377). Hershey, PA: Medical Information Science Reference. doi:10.4018/978-1-4666-3990-4. ch018.

Novas, N, López, JA, Gázquez, JA and Peralta, J (2004). Unidad cifrador/descifradora de mensajes con información digital, sistema y método de cifrado/descifrado para comunicaciones digitales en tiempo real. *ES patente* 2,272,130. 2004 Abril 16.

Ogedegbe, C, Morchel, H, Hazelwood, V, Chaplin, WF and Feldman, J (2012). Development and evaluation of a novel, real time mobile telesonography system in management of patients with abdominal trauma: Study protocol. *BMC Emergency Medicine*, 12, art. no. 19.

Salvador, CH, Ruiz-Sánchez, A, de Mingo, MAG, Carmona-Rodríguez, M, Carrasco, MP, Sagrado, PG, Fragua, JA, Caballero-Martinez, F, García-López, F, Márquez-Montes, JN and Monteagudo, JL (2008). Evaluation of a Telemedicine-Based Service for the Follow-Up and Monitoring of Patients Treated With Oral Anticoagulant Therapy. *IEEE Transactions on Information Technology in Biomedicine*, 12(6), 696-706. doi: 10.1109/TITB.2008.910750.

Sørensen, JT, Terkelsen, CJ, Nørgaard, BL, Trautner, S, Hansen, TM, Bøtker, HE, Lassen , JF and Andersen, HR (2011). Urban and rural implementation of pre-hospital diagnosis and direct referral for primary percutaneous coronary intervention in patients with acute ST-elevation myocardial infarction. *European Heart*, 32, 430–436.

Tripodi, A (2013). Results expression for tests used to measure the anticoagulant effect of new oral anticoagulants. *Thrombosis Journal*, 11, 9. doi:10.1186/1477-9560-11-9.

Uchino, K and Hernandez, A (2012). Dabigatran Association with Higher Risk of Acute Coronary Event. Meta-analysis of Noinferiority Randomized Controlled Trials. *Arch Intern Med*, 172(5), 397-402. doi:10.1001/archinternmed.2011.1666.

Van den Besselaar, AMHP, Poller, L and Tripodi A. (1999).World Health Organization (WHO) Guidelines for thromboplastins and plasma used to control oral anticoagulant therapy. *WHO Technical Report*, 889, 64–93.

Van der Werf, F, Brueckmann, M, Connolly, SJ, Friedman, J, Granger, CB, Härtter, S, Harper, R, Kappetein, AP, Lehr, T, Mack, MJ, Noack, H and Eikelboom, JW (2012). A Comparison of Dabigatran etexilate with warfarina in patient with mechanical heart valves. *Am Heart J*, 163(6), 931-937.

Walter, S, Kostpopoulos, P, Haass, A, Helwig, S, Keller, I, Licina, T, Schlechtriemen, T, Roth, C, Papanagiotou, P, Zimmer, A, Vierra, J, Körner, H, Schmidt, K, Romann, M-S, Alexandrou, M, Yilmaz, U, Grunwald, I, Kubulus, D, Lesmeister, M, Ziegeler, S, Pattar, A, Golinski, M, Liu, Y, Volk, T, Bertsch, T, Reith, W and Fassbender, K (2010). Bringing the hospital to the patient: First treatment of stroke patients at the emergency site. *PLoS ONE*, 5(10), art. no. e13758.

Wootton, R. (2001). Telemedicine. *Bmj*, 323(7312), 557-560.

Wu, T-C, Nguyen, C, Ankrom, C, Yang, J, Persse, D, Vahidy, F, Grotta, JC and Savitz, SI (2014). Prehospital utility of rapid stroke evaluation using in-ambulance telemedicine: A pilot feasibility study. *Stroke*, 45(8), 2342-2347.

Yu Hu, Stoelting, A, Yi-Tao Wanng, Yi Zou and Sarrafzadeh, M (2010). Providing a cushion for wireless healthcare application development. *IEEE Potentials*, 29(1), 19–23.

Table captions

Table 1. Statistics of INR* (International Normalised Ratio) measurements in ambulance and laboratory on subjects with and without oral anticoagulant therapy (OAT).

Patients	Nº of cases	Measurements in the ambulance		Measurements in the laboratory	
		Average	Standard Deviation	Average	Standard Deviation
Without OAT	19	1.09	0.02	1.06	0.02
With OAT	5	2.45	0.19	2.38	0.21

* It is referred for the measuring of prothrombin time in the plasma clot after the addition of the tissue factor.

Figure captions

Fig. 1. TeleAmbulance system architecture.

Fig. 2. Flowchart of the task INR of the mobile unit.

Fig. 3. Mobile unit equipment: a) Unit of communication and information processing, b) INR device and c) Medical monitor.

Fig. 4. Flowchart of t the repeat unit.

Fig. 5. SCADA application of INR data receiving.

Fig. 6. Flowchart of the tasks of the receiver unit.

Fig. 7. Packet of fixed size with variable fields; a: Original packet with the medical monitor biomedical data; b: Modified packet with all of the biomedical data.

Fig. 8. Data packet structure of INR. a: Packet of INR test request; b: Packet of answer with the sample obtained.

Fig. 9. Statistical quality in dynamic tests for the path UAL-HTC.

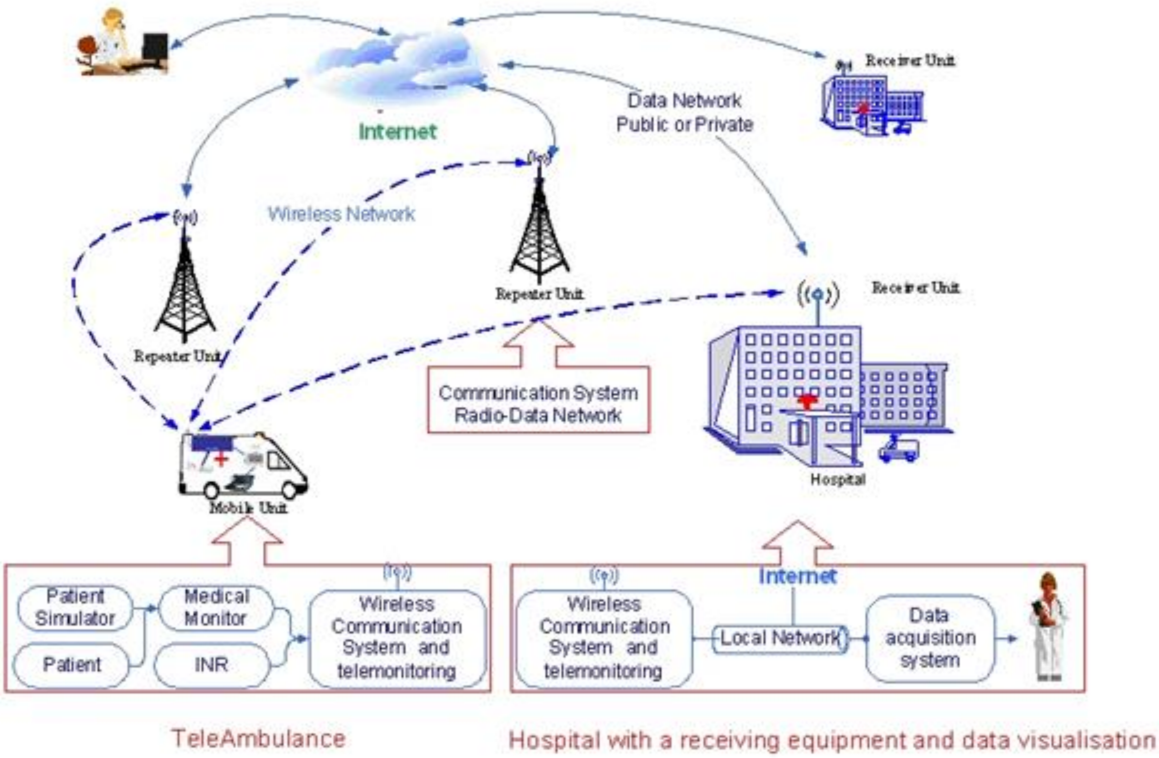

Fig. 1. TeleAmbulance system architecture.

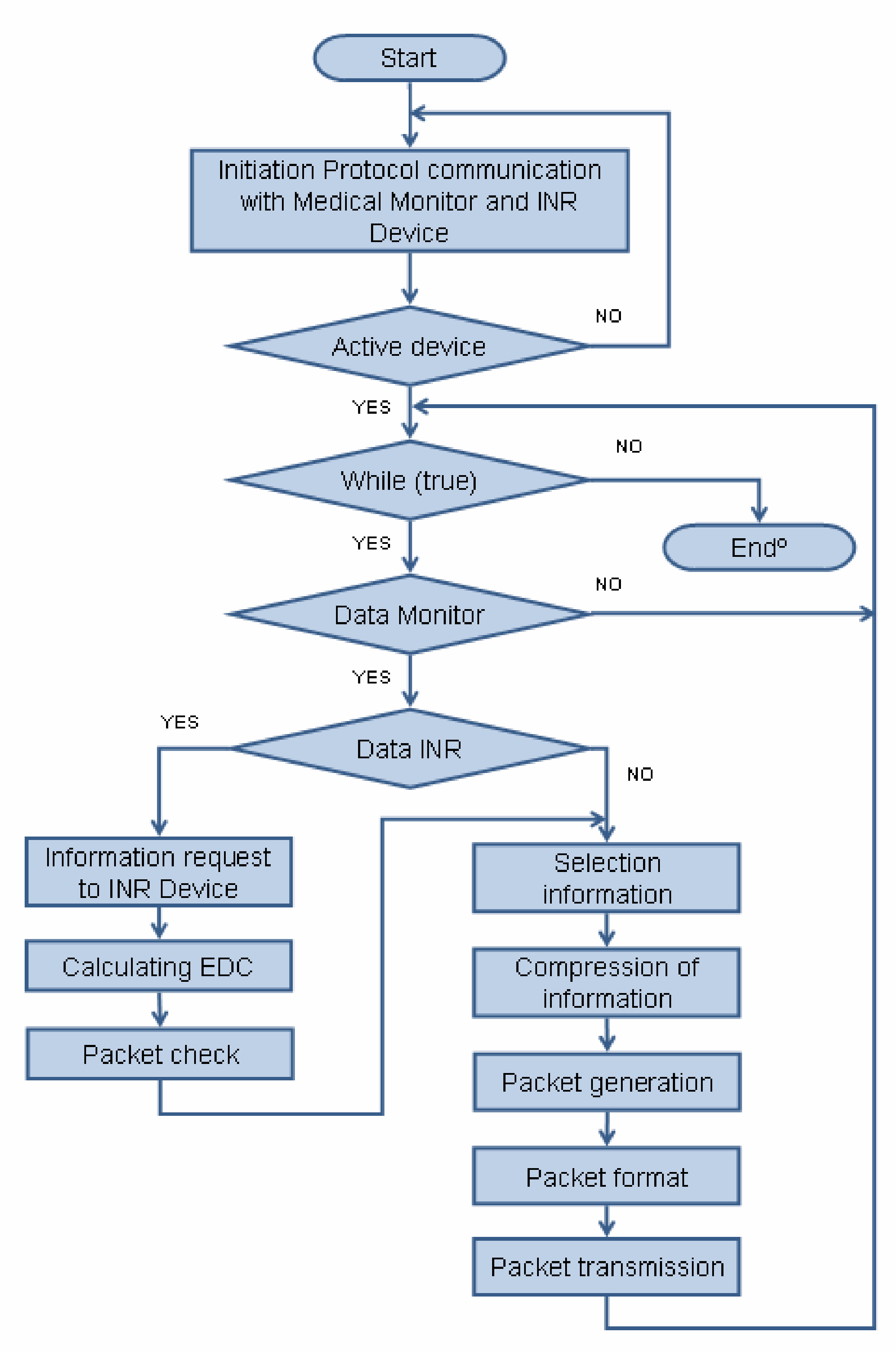

Fig. 2. Flowchart of the task test INR of the mobile unit.

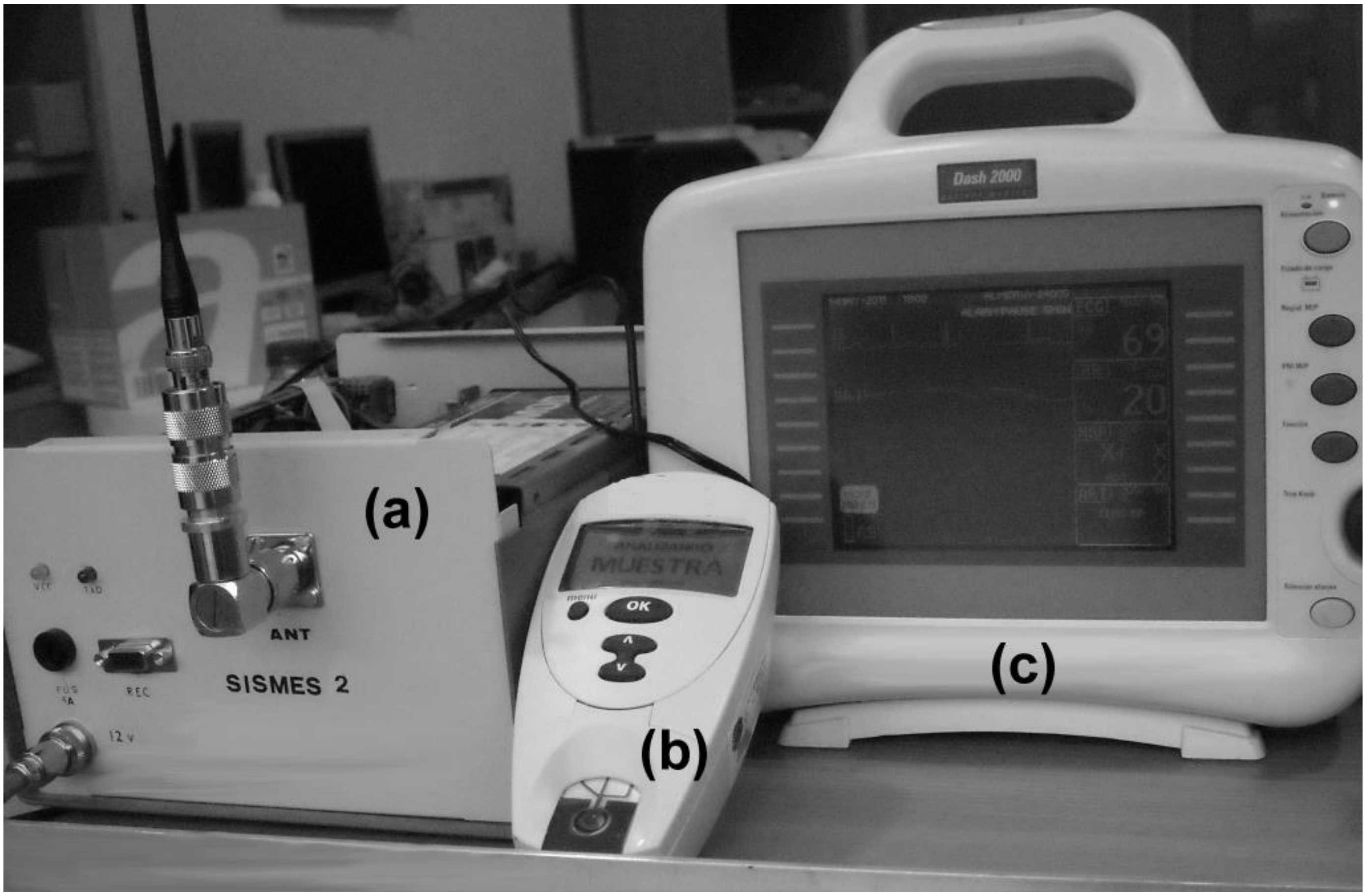

Fig. 3. Mobile unit equipment: a) Unit of communication and information processing, b) INR device and c) Medical monitor.

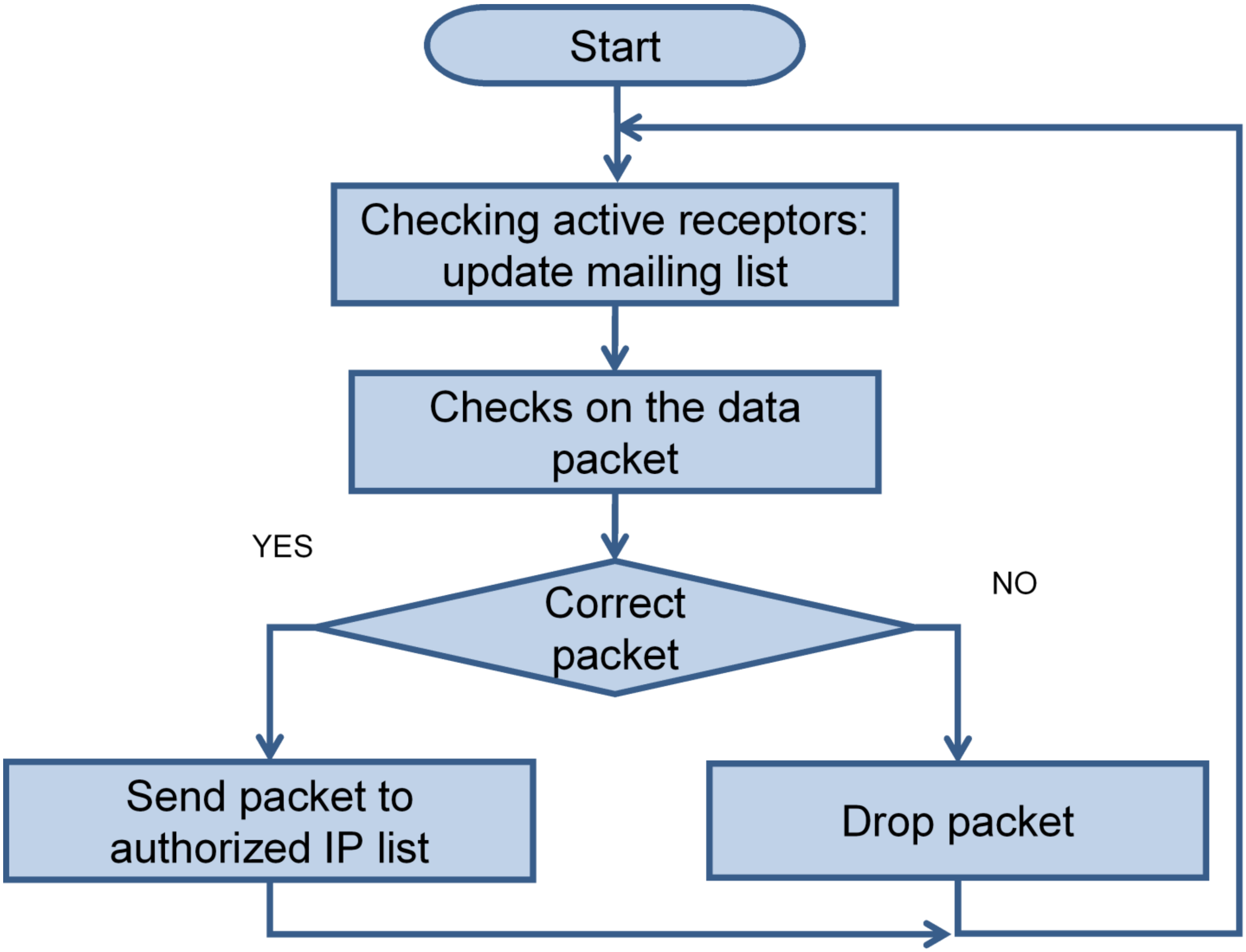

Fig. 4. Flowchart of the repeat unit.

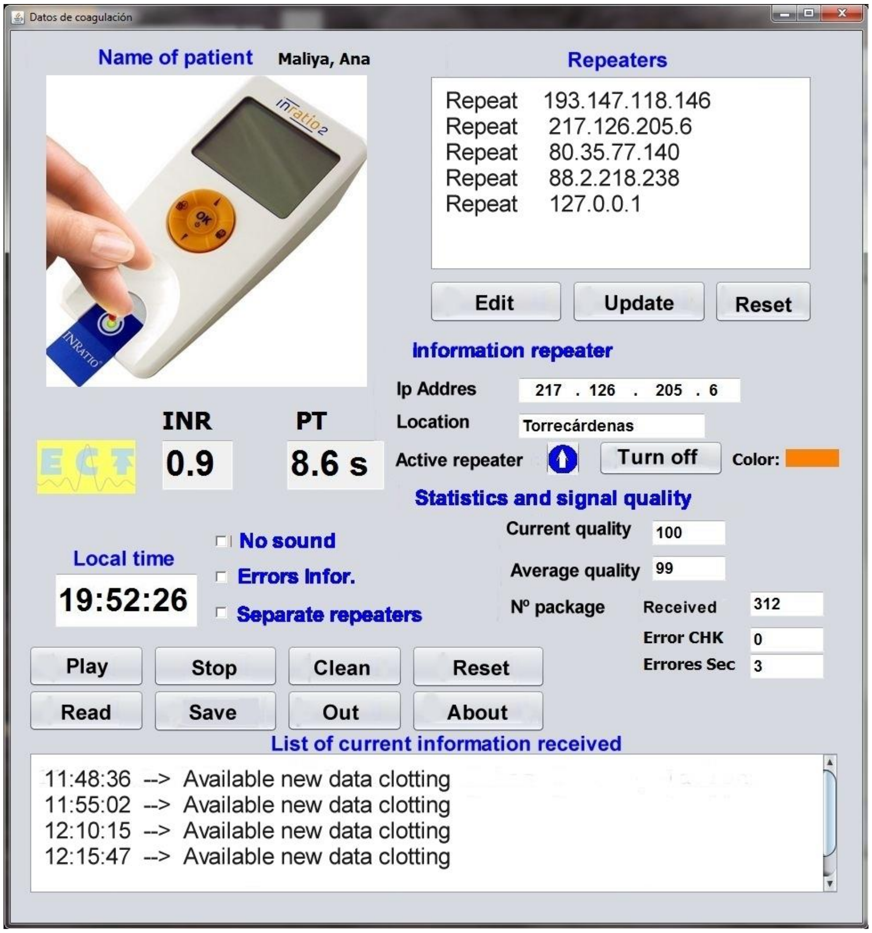

Fig. 5. SCADA application for INR data receiving.

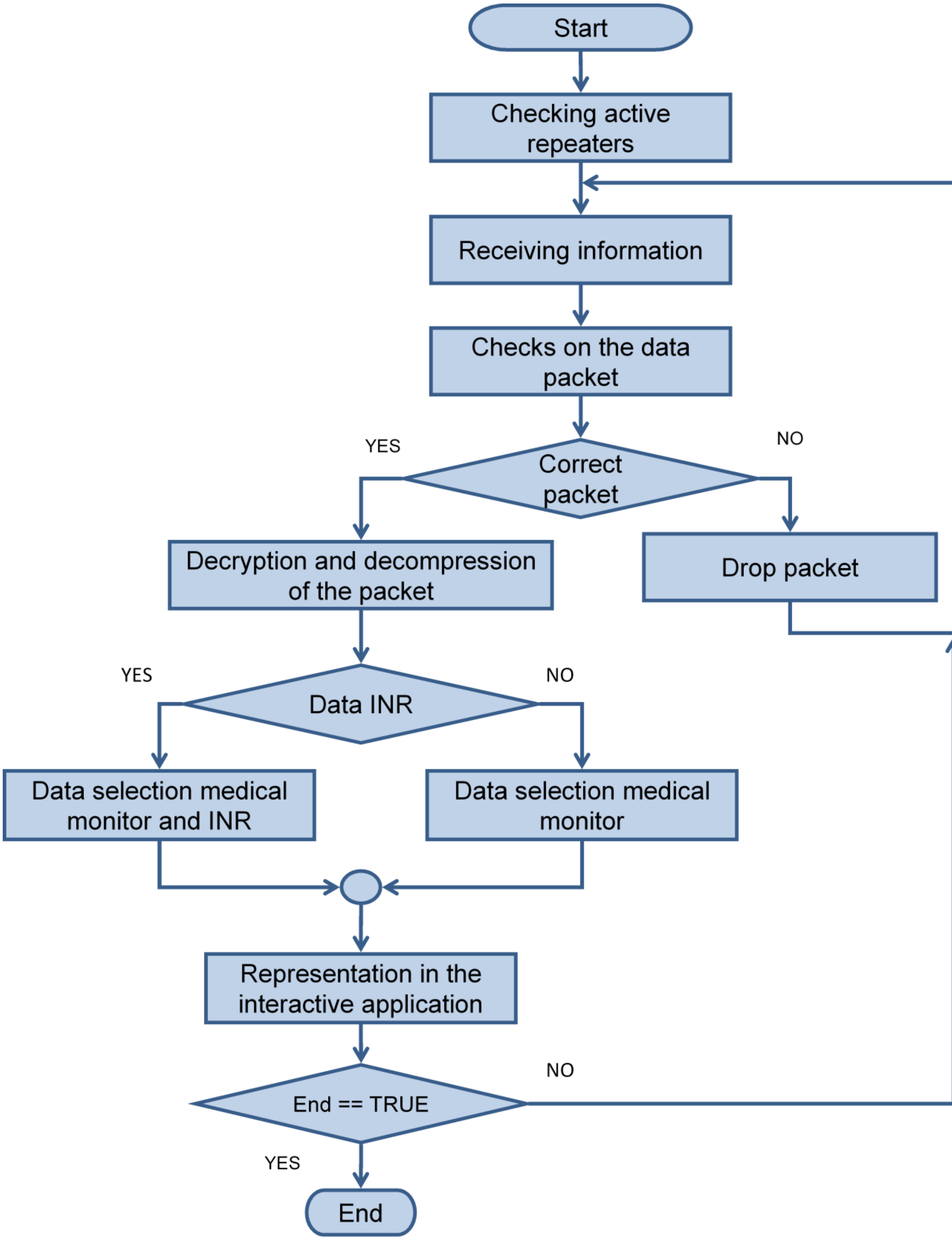

Fig. 6. Flowchart of the tasks of the receiver unit.

.

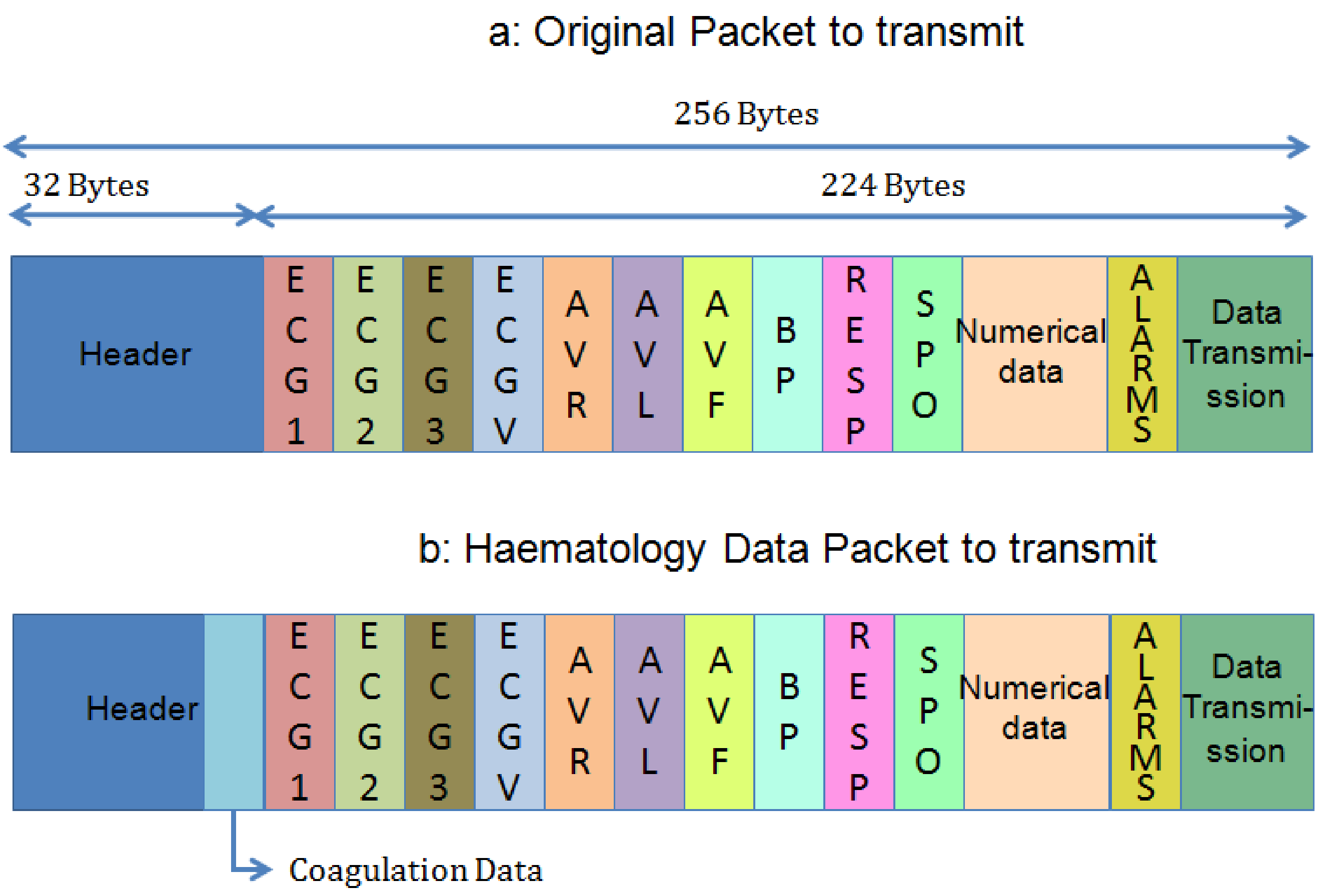

Fig. 7. Packet of fixed size with variable fields; a: Original packet with the medical monitor biomedical data; b: Modified packet with all of the biomedical data.

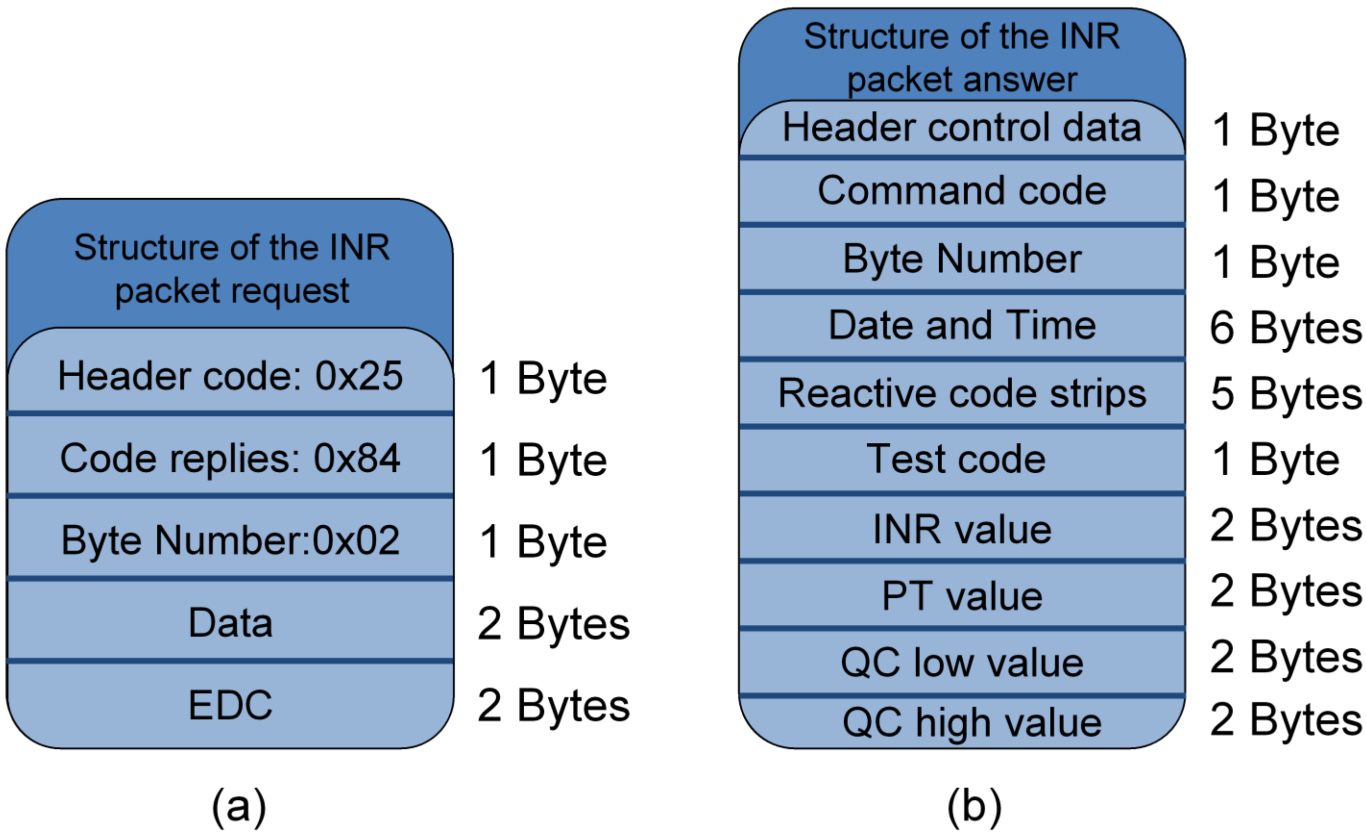

Fig. 8. Data packet structure of INR. a: Packet of INR test request; b: Packet of answer with the sample obtained.

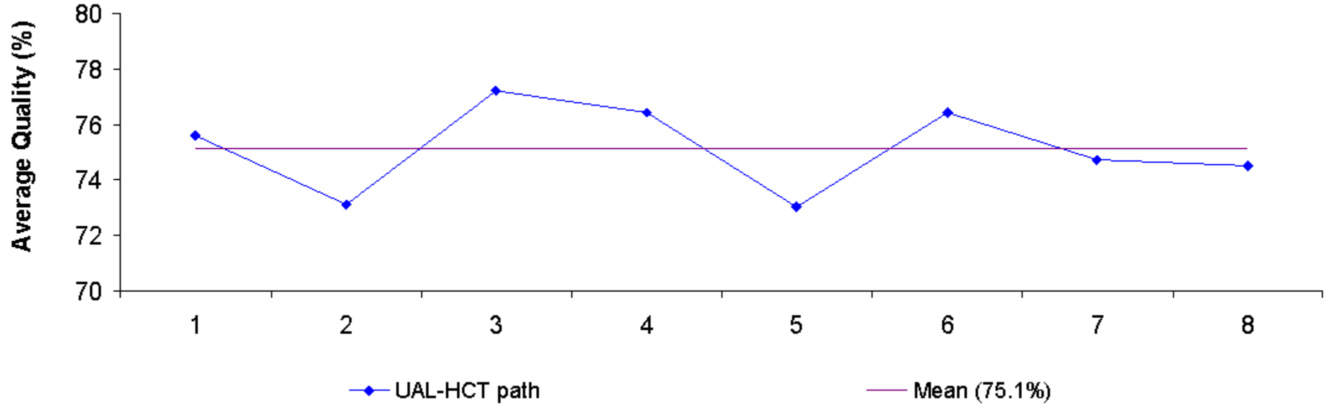

Fig. 9. Statistical quality in dynamic tests for the path UAL-HTC.