Employment of Telemedicine in Emergency Medicine

Clinical Requirement Analysis, System Development and First Test Results

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Summary

Objectives: Demographic change, rising comorbidity and an increasing number of emergencies are the main challenges that emergency medical services (EMS) in several countries worldwide are facing. In order to improve quality in EMS, highly trained personnel and well-equipped ambulances are essential. However, several studies have shown a deficiency in qualified EMS physicians. Telemedicine emerges as a complementary system in EMS that may provide expertise and improve quality of medical treatment on the scene. Hence our aim is to develop and test a specific teleconsultation system.

Methods: During the development process several use cases were defined and technically specified by medical experts and engineers in the areas of: system administration, start-up of EMS assistance systems, audio communication, data transfer, routine tele-EMS physician activities and research capabilities. Upon completion, technical field tests were performed under realistic conditions to test system properties such as robustness, feasibility and usability, providing end-to-end measurements.

Results: Six ambulances were equipped with telemedical facilities based on the results of the requirement analysis and 55 scenarios were tested under realistic conditions in one month. The results indicate that the developed system performed well in terms of usability and robustness. The major challenges were, as expected, mobile communication and data network availability. Third generation networks were only available in 76.4% of the cases. Although 3G (third generation), such as Universal Mobile Telecommunications System (UMTS), provides beneficial conditions for higher bandwidth, system performance for most features was also acceptable under adequate 2G (second generation) test conditions.

Conclusions: An innovative concept for the use of telemedicine for medical consultations in EMS was developed. Organisational and technical aspects were considered and practical requirements specified. Since technical feasibility was demonstrated in these technical field tests, the next step would be to prove medical usefulness and technical robustness under real conditions in a clinical trial.

1. Introduction

In life-threatening emergency cases implementing an early and specific therapy is important to achieve the best possible clinical outcome. The so-called chain of survival is usually initiated by an emergency call. The sending of adequate resources by a local emergency dispatch centre is the next link in the chain. This is often rather challenging, since frequently little well-certified evidence is provided by the caller. To ensure high quality in emergency medical services (EMS), highly trained personnel and well-equipped ambulances are needed. They should arrive on the scene within a reasonable period of time, which is the next important link in the chain. The specified help period (goal time for arrival) for EMS in Germany ranges from eight (populous Hamburg) to 17 minutes (sparsely populated regions of Thuringia). These time periods are statutorily regulated at the federal and state level for the “first adequate vehicle” arriving at the scene which is normally equipped with a paramedic team; partially divergent demands are predefined for metropolitan and rural regions considering the varying population density and infrastructure, respectively. Coincidentally, experience of medical staff in managing severely ill and severely injured patients is considerably lower in rural regions due to the far lower number of such emergency cases. However, quality depends on both formal qualification and experience [1–3]. Consequently in the mentioned regions, latency to the onset of therapy is typically higher and quality of
medical treatment generally lower. In several European countries including Germany, a dual system for emergency response with both EMS physicians and paramedics has been established; usually they are dispatched separately. Several studies have shown that at least critically ill patients benefit from treatment by an EMS physician [4], particularly in cases of cardiopulmonary resuscitation, advanced airway management, further invasive procedures, well-directed fluid management and early pharmacotherapy [5–7]. In summary, EMS with physicians are often considered to be superior in literature [1, 3]. In Germany, paramedics have restricted competencies in invasive procedures and intravenous medication, depending on local regulations. Since ambulance stations are more closely meshed than EMS physician locations, a time gap can occur in which paramedics have to wait for a doctor due to their restricted competencies. Depending on the characteristics of a particular case, time delay of treatment might prove disastrous.

In addition to the above, several facts lead to increasing problems in ensuring high quality in prehospital medical care. Due to demographic changes and steady improvements in medical treatment, patients have become older with more comorbid conditions but more frequently get outpatient treatment. Hence, the number of emergency cases is rising and professional demands are increasing [8] to such an extent that a deficiency of qualified EMS physicians has resulted, particularly outside of major cities [9]. The previously mentioned challenge of emergency control centres in dispatching adequate resources leads to the unnecessary deployment of EMS physicians and, therefore, to further aggravation of this deficiency. In practice, several scenarios have to be considered.

First scenario: ambulance and EMS physicians are dispatched at the same time, but the ambulance reaches the scene earlier. This is a very frequent occurrence due to the higher number and regional distribution of ambulance stations. Since no doctor is present but already dispatched, the aim of tele-consultation is to minimize time to treatment. Regarding legal effects and ethical considerations this is the easiest case since currently there is no alternative present.

Second scenario: only an ambulance is initially dispatched. After initial evaluation, the paramedics decide to call for a physician. The tele-EMS physician can carry out an own medical diagnosis and provide medical advices and instructions without any delay. Finally, the major difference to the first scenario is that the tele-EMS can affect the disposition of further facilities such as the emergency physician.

Third scenario: again only an ambulance is initially dispatched. Although there is no life-threatening situation requiring the physical presence of a physician, there is a special medical enquiry. Medical or organizational advice or recommendation can be provided by a tele-EMS physician. The particular challenge of this scenario is that the involved tele-EMS has to evaluate the special situation quickly to decide whether the absence of a doctor on-site is acceptable and reasonable regarding legal and ethical considerations before tele-consultation.

Fourth scenario: a team of paramedics and EMS physician is involved together in handling a very tricky or complex medical case. A second medical opinion or recommendations by a more experienced specialist can be provided by teleconsultation. The on-site located doctor bears responsibility.

The four scenarios described previously highlight the emerging potential of telemedicine to improve EMS. According to Pfeiffer [10], medical informatics plays a major role in this field. It should focus on strategic concepts to develop innovative information and communication technology solutions for the health care system [10].

In order to analyse the potential benefits of telemedicine, it is necessary to emphasize certain typical functions of an EMS physician: 1) a physician’s knowledge is required to decide on initial treatment; 2) medical decisions are necessary to enable early therapy and rational referral for further treatment; and 3) physical skills or manual support are required. Telemedicine is a potential option in the case of the first two points. Both a lack in personnel resources and the technical advances in mobile equipment have led to significant developments in telemedicine during the last years. A number of projects have demonstrated that telemedical applications can provide expertise at the scene and improve the quality of the medical treatment [11–15]. Recently a combination of real-time tele-stethoscopy and videoconferencing was found to be a helpful tool [16]. In a recent pilot study, we have shown that teleconsultation in EMS with acceptable performance was feasible. However, the currently used telemedicine systems in EMS still demonstrate various technical problems [17, 18]. Moreover, except for ECG transmission to a cardiology department, telemedicine is not yet an established practice but is mostly in a state of trial. The major challenge in EMS is that specific circumstances at the scene of an emergency are not predictable and so the existing infrastructures available at the scene, such as the mobile communication conditions, are totally unclear – particularly in rural areas. Another challenge is that the requirements for robustness are much more sophisticated – systems must be able to resist extreme weather conditions, careless handling and technically under-trained staff. Additionally, to reach high feasibility and user compliance, developed systems must be physically small, lightweight and at best integrated into existing devices.

2. Objectives

The aim of this project is to analyse requirements for the use of telemedicine in EMS in terms of hardware, software and organizational issues, to develop a robust and reliable system fulfilling defined requests and, finally, to carry out preliminary performance tests in preparation for future more specific clinical studies.

3. Methods

3.1 Requirement Analysis

An adequate requirement analysis is crucial to obtain useful final outcomes and should be an integral part of the system development process. Therefore physicians and paramedics, who are the intended end-users, and software and hardware engineers collaborated on our project. Experienced EMS physicians were chosen to guarantee a high practical level of commit-
ment and a high practical concern. We decided to define certain use cases to specify requirements for the following groups: system administration, start-up of EMS assistance system, audio communication, data transfer, routine tele-EMS physician activities and research capabilities. Use cases can be classified as: 1) routine activities performed during most consultations; 2) routine, daily activities; and 3) occasional activities required under specific circumstances.

Hence, the major features requested were:

- robust and reliable audio connection between tele-EMS physician and the on-site team;
- robust and reliable vital data transfer;
- photography and video acquisition where adequate network infrastructure is available;
- documentation and reporting of tele-consultation.

Besides, development of standard operating procedures with regard to organizational matters but also concerning medical treatment was specified.

3.2 Testing Concept

After extensive regular technical tests during the development process, additional field tests involving medical users in more realistic environments are needed. On the one hand, the connection of diverse hardware and software components to one system is complex and error prone; on the other hand, practical requirements regarding robustness, feasibility and usability are extremely high in EMS. Since communication between ambulances and tele-EMS physicians is based on mobile communication, it is highly dependent upon available network infrastructure, which is not foreseeable in emergency cases. Regions where the system would be finally implemented were chosen for our testing scenarios (Figure 1). Testing locations were both urban and rural so that different technical conditions were experienced. Apart from technical infrastructure, the impact of weather, temperature and vibrations is of high relevance in real operating conditions. Hence, technical field tests were performed under as realistic conditions as possible, using the original devices, ambulances and diverse test sites. The test scenarios were iteratively developed and performed with two physicians and up to four engineers in attendance so that both sets of competences were available both at the TC (tele-consultation centre) and on the scene. Al-

![Figure 1](https://example.com/fig1.png)  
**Figure 1** Overview of testing sites. Sites for technical field tests (circles) were chosen with regard to designated locations for future implementation (diamonds). However, main emphasis was changed to regions with poor coverage of mobile phone networks.
though this test setting does not represent the reality, it allowed best interaction between technicians and clinicians during the tests. During approximately one month (14th June to 20th July, 2012), 55 test scenarios with partly different purposes were assessed. The time needed to establish various system features (end-to-end measures), the location of the test scenario and the quality and availability of mobile communication technologies were all assessed ( ►Table 1).

4. Results

4.1 Overview of System Design

In an interdisciplinary process a team of experienced EMS physicians, paramedics, engineers and software developers defined 24 use cases which were the basis for the system development process.

The most frequently used features are expected to be the handling (initializing, refusing and forwarding) of audio communication (urge and routine), vital data (ECG, oxygen saturation and blood pressure), photo and video transmission as well as generating and printing medical consultation reports.

Regarding audio calls, a distinction was made between two different kinds of incoming calls: high priority calls for urgent consultation and standard calls for non-critical communication. Depending on the situation, assessment and transmission of various data is often crucial for an adequate teleconsultation. Vital data can be continuously or periodically transmitted. Therefore, both cases were considered – continuous transmission of vital data, such as ECG curves, heart rate (obtained from plethysmography or ECG), oxygen saturation and capnography, as well as periodical vital data transmission (auscultation using an electronic stethoscope, photography, video acquisition and cardiocography). Additional daily features deals with administration of emergency cases, reporting facilities and medical documentation of the teleconsultation. A complex infrastructure concept was developed based on the described requirements ( ►Figure 2).

In particular, six conventional ambulances were equipped with telemedical facilities. Both, portable and fix mounted in-vehicle version, autonomous communication devices called the “PeeqBOX” (P3 communications, Aachen, Germany) have been developed based on the underlying requirement analysis. Basic technical details of this device will be described in the next subsection. Additionally an integrated in-car PC based on the PeeqBOX architecture was employed as an additional transmission unit. A camera was fixed to the ceiling (SNC-RZ 50P, Sony Electronics Inc., San Jose, CA, USA) providing real-time video streaming of the ambulance interior via direct connection to the in-car PC. Furthermore, a camera user interface, which can be directly used by the tele-EMS physician, provides features such as zooming, tilting and rotating. An in-car printer (Brother Pocketjet PJ-623, Brother Industries Ltd, Nagoya, Japan) connected via local area network (LAN) allows the tele-doctor to print out documents such as protocols.

4.2 Hardware

Since most of the highly relevant clinical data is assessed by the patient monitor/defibrillator unit, this device plays a major role in general emergency handling and, therefore, also in our communication network. The portable PeeqBOX, weighing 1.8 kg, was attached and connected to the Philips MRx monitor (Philips Healthcare, Andover, MA, USA) via LAN and Bluetooth to transfer real-time vital data (non-invasive blood pressure, numerical values and curves of ECG rhythms and pulse oxymetry), 12-lead ECG and periodical vital data (package files) to be transmitted to the tele-EMS physician. A smartphone (HTC Desire, High Tech Computer Corporation, Taoyuan, Taiwan) was also used: still pictures taken with its camera application were automatically transferred to the PeeqBOX via Bluetooth and then forwarded to the TC through mobile networks. The mobile phone also acts as a backup for the audio connection. The portable PeeqBOX provides an optimal internet connection by enabling the use of up to three mobile network providers simultaneously. Inside the ambulance, data transmission switches to the in-car transmission unit using roof antennas and enabling the
The use of up to five mobile networks simultaneously. Apart from data trunking, the PeeqBOX also provides encryption and security. Finally, the transmission of real-time vital data requires high internet bandwidth. Generally third generation (3G) networks are beneficial but second generation (2G) networks are mostly sufficient for transferring smaller data packages such as periodical datasets.

Energy consumption was another challenge addressed in the development process. A useful feature to reduce power usage was achieved as follows: PeeqBOX system shutdown is initialized when the ambulance is at its station or at a (preregistered) hospital (by means of the Global Positioning System) for more than 10 minutes. When turned off, the acceleration of the ambulance in motion causes the system to boot up after 10 seconds. A battery change might be necessary during a shift of eight hours depending on usage.

A TC was set up with specialized and highly experienced tele-EMS physicians offering telemedical assistance. In addition to the predefined minimum requirement with regard to education (medical specialist, senior emergency physician for mass casualties, European Resuscitation Council (ERC) Provider, Advanced Trauma Life Support (ATLS) or Pre Hospital Trauma Life Support (PHTLS) Provider and Pediatric Advanced Life Support (PALS) Provider), all tele-EMS physicians received training specific to telemedical peculiarities and communication principles. Since medical consulting is based on available data, capabilities are dependent on mobile networks. In cases of at least one 3G network with sufficient signal strength, all data could be transferred in real-time. Medically approved software (IntelliVue Information Center, Philips Healthcare, Boeblingen, Germany) was used for the visualization of real-time data curves. The HeartStart Telemedicine Viewer (Philips Healthcare, Andover, MA, USA) was used for 12-lead-ECGs. In cases where real-time transmission was impossible, periodical data mode providing numerical vital data measures and periodical ECGs each minute can be selected.
4.3 Software

The documentation software was developed in a very close collaboration between the tele-EMS physicians and software engineers. The aim was to create a user-friendly graphical user interface while fulfilling legal and practical requirements of medical documentation. The very common ABCDE and SAMPLE algorithms were employed for this purpose, guiding the user through the medical focus (A: airway, B: breathing, C: circulation, D: neurological deficits, E: environment, further examination) and concomitant conditions (S: symptoms, A: allergies, M: medication, P: premedical history, L: last meal, E: environment).

Based on international guidelines and recommendations, medical standard operating procedures (SOPs) were developed for the following emergency situations: bronchial asthma, chronic obstructive pulmonary disease, hypoglycaemia, acute coronary syndrome, hypertensive emergency, acute pain therapy (traumatic and non-traumatic) and stroke. To this end, national and international guidelines were investigated, studied and partially adapted to the peculiarities of telemedical consultation. Quality assurance was implemented through these SOPs – medical treatment was imposed according to the current state of science. Moreover, organizational SOPs were developed for further standardization, structuring system start-up, daily routine procedures and troubleshooting. The SOP database was integrated into the documentation software.

4.4 System Performance Tests

As mentioned, fifty-five scenarios were tested and analysed throughout a period of one month. The involved doctors (at age 33 to 44) who defined the scenarios and carried out the tests were highly experienced in EMS (assigned for EMS physicians for 3 to 14 years; previous experience as paramedics for up to 12 years). Usability and robustness of the tested devices as well as of the developed software for the tele-EMS physician were satisfactory. Availability of mobile communication and data networks differed extensively (Table 2), particu-

### Table 2
Availability of mobile networks. In addition to the availability of 3rd generation mobile networks also signal strength matters. During the technical field test, SIM cards of three providers were used that showed regionally diverging performance. This table shows the results regarding availability of mobile networks during 48 test cases. For the remaining seven test scenarios no information about mobile networks was available due to technical reasons. GSM: Global System for Mobile Communications; UMTS: Universal Mobile Telecommunications System.

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<th>Provider 1</th>
<th>Provider 2</th>
<th>Provider 3</th>
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<tbody>
<tr>
<td>GSM</td>
<td></td>
<td></td>
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<tr>
<td>Number of test cases</td>
<td>18</td>
<td>19</td>
<td>7</td>
</tr>
<tr>
<td>% of total cases</td>
<td>37.5</td>
<td>39.6</td>
<td>17.0</td>
</tr>
<tr>
<td>Signal strength (%)</td>
<td>61 [61; 70]</td>
<td>48 [31; 64]</td>
<td>48 [42; 53]</td>
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<td>UMTS</td>
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<tr>
<td>Number of test cases</td>
<td>30</td>
<td>29</td>
<td>34</td>
</tr>
<tr>
<td>% of total cases</td>
<td>62.5</td>
<td>60.4</td>
<td>83.0</td>
</tr>
<tr>
<td>Signal strength (%)</td>
<td>53 [33; 63]</td>
<td>64 [45; 70]</td>
<td>43 [32; 63]</td>
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larly between rural and urban regions. Interestingly, mobile communication provider number three offered a 3G mobile network significantly more frequently, but signal strength was often lower. As a matter of fact signal strength and UMTS availability were significantly lower in indoor conditions compared to outdoor conditions. At least one UMTS network was available in 76.4% of test cases. Periodic transmission of vital data (each minute) and real-time audio communication showed acceptable quality even with GSM technology and lower signal strengths. System information about the availability of mobile networks was given during 48 test cases; for the remaining seven test scenarios no information about mobile networks was available due to technical reasons.

The required time for various functionalities based on our test protocol was measured end-to-end. The most important feature, initiation of an audio call, took a median of 7.3 seconds (range 6–29 s) when requested by the ambulance team and 18 seconds (range 6–38 s) when requested by the tele-EMS physician. Interestingly, changing vital data transmission from continuous to periodic mode took significantly longer than vice versa. Generally the time needed for still picture transmission (median 51.5 s (range 12–437 s)) was shorter than for 12-lead ECG transmission (median 119 s (range 74–213 s)) (Figure 3); consequential data rates varied between 2 kB/s and 26 kB/s and the average photo file size was 658 kB (26–1552 kB).

Even though 3G mobile cellular systems such as UMTS provide beneficial conditions for higher data rates, signal strength is also essential. During the tests, availability of mobile service providers varied (Figure 4). Transmission of larger data packages such as photos or 12-lead ECGs tended to take less time when UMTS was available: median 84 seconds vs. 100 s for photo transfer; median 120 s vs. 137 s for ECG transfer.

Quality of voice communication was in median 2 (good), ranging from 1 (excellent) to 4 (adequate); quality of vital data transmission was 1 (on a range of 1 to 3.5) and video transmission was also rated as 1 (on a range of 1 to 3) where possible.

5. Discussion

A multifunctional teleconsultation system for emergency cases was developed and tested after an appropriate requirement analysis. Apart from the integration of components into the ambulance, development of mobile technical devices and setup of a TC, specifically adapted controlling and documentation software was also developed. Three major site types should be defined from the organizational point of view: emergency sites such as inside or outside of buildings, patient handling inside the ambulance and the TC.

It is impossible to predict emergencies – neither their time and location nor their specific challenges and circumstances. Conditions are often unfavourable and available room limited so that medical treatment is hampered. Personnel have to concentrate on medical treatment; maintenance and operation of technical devices have to be as simple as possible. Hence, the main desired properties regarding the handling of emergency cases are mobility, robustness and practicability.

Although meaningfulness of a teleconsultation system for emergency medicine was already demonstrated with a precursor of the system in previous studies [17], technical performance and reliability were not completely satisfactory due to malfunctions and failures. Aspects of practicability were also addressed by reducing the total weight of the communication unit from 12 kg to 1.8 kg and by integrating it into the bag of the patient monitor/defibrillator unit.

Naturally the bottleneck of data transfer to the TC is the available mobile network, especially indoors in more rural locations. Thus, an adapted system that permits using or omitting certain components such as real-time data transmission is potentially beneficial.

In the ambulance, connection is considerably more stable due to lacking build-
ing insulation and the use of outdoor antennas. Therefore, data transfer rate was usually higher for patient handling in the vehicle, allowing stable real-time video and vital data transmission.

The focus for the TC is on developing reliable software with user-friendly graphical user interfaces. Additionally, the ability to distinguish between malfunctions occurring in supported ambulances or on emergency sites respectively plays an important role. Since the TC desktop consists of diverse combined software systems each related to one site, the danger of confusion should be considered.

Medical and organizational SOPs for both TC and remote site must ensure quality assurance and standardized handling according to current guidelines.

Of course, besides reliability and user-friendliness, overall system performance matters. In our first field test this was mainly tested with end-to-end measurements. Measured data rates are the result of a complex combination of circumstances, as it mixes the Bluetooth performance of different device combinations with mobile data transfer rates. Nevertheless the major influencing factor for system performance was indeed availability and quality of transmission channels. Hence, particularly in rural regions, data transfer requiring low latency communication such as real-time vital data transmission does not work adequately. However, several consulting features could be recovered by switching to periodic transmission mode. Periodic transmission (each minute) of vital data and real-time audio communication showed acceptable quality even with GSM technology and lower signal strengths. Since it took much longer to change the mode from continuous to periodic than the other way around, an early evaluation and decision should be arrived at soon enough in cases of severely impaired signal quality and/or lacking 3G mobile networks. Furthermore, both the tele-EP and the ambulance team should use technical features carefully in order to optimize information flow.

With regard to the audio connection, certainly the most important feature, at least satisfactory results were achieved even under poor conditions. Calling the TC from the remote site could be accomplished within several seconds (the opposite also applies) and speech quality was mainly rated as good or excellent.

Sending photos from the remote site was partly problematic when performed under poor network conditions – this process took up to 7 minutes and could lead to congested data channels in the meantime. Additionally, the problem lies with the data compression of images, which varies depending on the image content. The tele-EMS physician and involved paramedics should observe the status lights of the PeeqBOX that inform about signal strength and the availability of services.

Several limitations have to be addressed with regard to the developed system and the performance test carried out. The adaptability of the whole system under conditions of poor connection plays a major role. Hence, in our point of view, the development of automatically adapting systems that enable or disable specific features according to the current network connection should be a future aim. Despite the implementation of innovative energy-saving algorithms, mobility highly depends on battery capacity and energy consumption, particularly that of the PeeqBOX.

No mobile network (2G, 3G) is yet available in some rural areas. Naturally, no teleconsultation is possible in such cases. Therefore, alternatives such as fourth generation mobile networks (Long Term Evolution; LTE) or satellite connectivity should be studied. The support of other communication technologies is possible from a technical point of view.

It is important to point out that the examined performance test scenarios do not fully represent real conditions. While the ambulance team and the tele-EMS physician focus on medical treatment during emergency cases, no injured patient was involved in the test cases. Moreover, involved testers were physicians and engineers and not common ambulance personnel. Nevertheless, realistic test scenarios and locations were chosen and medical staff who participated were highly experienced in EMS – partly with previous experience as paramedics.

Another limitation which should be addressed is that our system is partially proprietary based on the standards and demands of our project partners. In the medium term open interfaces and protocols should be defined so as to enable further manufacturers of medical rescue equipment to participate in our teleconsultation system. Moreover, open interfaces and standard protocols were already used such as IP over Ethernet, Bluetooth transfer and file transfer protocol.

6. Conclusions

In summary, a teleconsultation system including devices for the remote site and software for a tele-EMS physician operating from a teleconsultation centre that was reliable and usable under field test conditions was developed. Since the technical feasibility of teleconsultation has been confirmed, the next step is to prove medical usefulness under real conditions in a clinical trial. In our opinion the developed system provides an outstanding potential to overcome the growing lack of resources in emergency medicine in the future.

List of Abbreviations

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<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ABCDE</td>
<td>Airways, Breathing, Circulation, Neurological Deficits, Environment</td>
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<td>EMS</td>
<td>Emergency Medical Services</td>
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<tr>
<td>LAN</td>
<td>Local Area Network</td>
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<tr>
<td>LTE</td>
<td>Long Term Evolution</td>
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<tr>
<td>SAMPLE</td>
<td>Symptoms, Allergies, Medication, Premedical history, Last meal, Environment</td>
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<tr>
<td>SOP</td>
<td>Standard Operating Procedures</td>
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<tr>
<td>TC</td>
<td>Teleconsultation Centre</td>
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<tr>
<td>UMTS</td>
<td>Universal Mobile Telecommunications System</td>
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Competing Interests

Tadeusz Brodziak is executive development engineer from P3 communications GmbH, Aachen, Germany. His company invests own resources in the development of the PeeqBOX. Therefore financial interests cannot be denied. All other au-
Authors declare that they have no competing interests.

Authors’ Contributions

MC and SB designed the study, acquired data and drafted the manuscript. ST and TB acquired and analysed data from the technical point of view. BV, SKB and FH acquired and analysed data from the medical point of view. RR and JCB conceptualised and designed the underlying project and attracted funding. All authors read, revised and approved the final manuscript.

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References


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