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Editor's Corner

I am not sure to whom the credit is due for the saying - *Take pride in how far you have come and have faith in how far you can go!* But it is reflective of the feelings of most clinical engineers (CEs) including me – the pride of being a practicing CE.

I am routinely in continuous communication with professional colleagues all over the world. A couple of evenings ago, I was chatting with one such colleague who works in a mid-west hospital in the United States. He is known as a caring manager with vast experience. He is hardworking and expects no less from his CEs and biomedical equipment technicians. During our chats, he was never at a loss for words and always centered his talks on the latest sports scores (especially if his favorite team won) and about finding ways to collaborate with clinical, administration, and IT departments to improve his program's impact on patient care outcomes while at the same time saving on hospital expenses. After years of these conversations, I could predict the flow. The topics did not change much but the order did and there was a greater emphasis on his first passion – CE. He is a caring manager of the first kind.

However, a couple of nights ago, our chat was completely different. His conversation was short, there was no Monday morning quarterbacking or any sports chat at all. After a short while, I quickly realized that he was not himself. I asked him what was going on as I found him to be so different. His spirits were up but his response shocked me.

Myself, I practice CE in the largest medical center in the world (the Texas Medical Center) where we've been through hurricanes, floods, and evacuations. As far as I can remember, I had never witnessed a colleague's behavior turn as his did that evening. He shared the demands of his work that were similar to those that I

had been hearing from many other colleagues over the previous 14 weeks. During these abnormal times, he had been working an average of 10 hours a day almost seven days a week. He was lost in an environment created by the ever-changing knowledge around COVID-19, about its spread, diagnosis, care protocols, and the reality of shortages of equipment and supplies – and was constantly challenged to quickly come up with workarounds and safe solutions. But it was the second part that shocked me. There are many challenges around the reuse of single-use protective gear, to the support of multiple patients from a single ventilator, to devising isolation care spaces. At this point, he felt that maybe he was not doing enough for his patients. The burden was heavy. Successful solutions needed to be trialed and were expected in rapid succession, yet the resources of both qualified labor and appropriate technology were in short supply.

I know him and his program, it runs like a Swiss clock. Yet he was frustrated by not being able to do more. By any measure, he is one of the silent heroes, one of the CE professionals who use their competencies, experience, and open their hearts every day in the committed pursuit to provide safe and efficient patient-ready technology that supports the mission of their organization. CEs perform their many tasks all over the world 24×7×365 but their critical contribution mostly goes unrecognized. The CE profession has certainly evolved and has begun to enjoy more input into the needed and effective programs they provide and manage, especially during this present huge demand for CE knowledge and leadership. However, we still have a long way to go to increase the awareness of the public and medical decision-makers. They need to know that by including the unique expertise of competent CE practitioners within the healthcare system's decisions, improved safety and quality will follow. This will result in healthcare delivery that is more accessible to a larger volume of patients - that would not be possible otherwise.

It is no mistake that the *Journal* made the decision to dedicate our front-page cover to recognizing all CE professionals. These are the people that are working deliberately to maximize the availability of proper technology and ensure that care providers have what they depend on to manage and help their patients. In other words: to always have the needed safe technology in “patient-ready state,” always appropriately selected, and in optimal operational performance administered under frugal use of resources.

As you all know, this part we are already delivering. So, what else could a hospital administrator wish for? If they think of anything, we are listening!

BIG thanks to my colleagues and all the CE heroes all over the world!

Today, tomorrow, together!

Dr. Yadin David



CONTENTS

Editor's Corner	1
Proposed Calibration of Apheresis Equipment By A. A. dos Santos, M. A. Marciano and R. L. Rezer	4
Quality Certification of Medical Devices in Venezuela: Process Developed by Simón Bolívar University, Caracas-Venezuela By R Mijares, N. Utrera, Z. Sierra, S. González, R. Lugo, M. Rincón, R. Mijares	8
Semi-automatic 3-D Reconstruction Measurement of Muscle Volume with Magnetic Resonance Imaging By Q. Zhou, Q. Hu, X. Yang, Y. Chen, Y. Yu, J. Zhang, Q. Ma, G. Zhou, H. Wei, B. Zhang, H. Zhang	15
A Model for Priority Setting in Health Technology Innovation Policy By J. Sharma, J. Bunders, T. Zuiderent-Jerak, B. Regeer	24
Development of a Biomechatronic Device for Motion Analysis Through a RGB-D Camera By F. Pristerà, A. Gallo, S. Fregola, A. Merola	35
Bedside Communication and Management of Vital Parameters and Alarms In Care-Intensive Environments: Simulation Model Development for the Clinical Effectiveness Analysis of an Innovative Technology By I. De Rosa, A. Pepino, G. Giaconia, M. Guarino	45

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Proposed Calibration of Apheresis Equipment

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ABSTRACT

The health establishment is currently developing quality control through the calibration of biomedical equipment, systematically and comprehensively throughout the wide range of available hospital technology. Thus, this work aims to propose and demonstrate a method of qualifying apheresis equipment through equipment calibration before releasing it for first-time use. Results show the values obtained in calibration of apheresis equipment, relating to the MNC protocol (removal of mononuclear cells), the pressure of access, and return pressure.

Keywords – *Qualification of Incorporation, Biomedical Equipment, Calibration of Apheresis Machines.*

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INTRODUCTION

Among the human pathologies are hematological diseases, immunodeficiency, genetic diseases and some tumors such as from breast cancer. One of the available treatments is donor (autologous) and donor (allogeneic) donor transplantation of peripheral blood progenitor cells. These cells, classified as CD34 +, have a high capacity for self-renewal and proliferative potential, which makes it possible to differentiate them into progenitor cells from all blood strains and to reconstitute the population from a single cell hematopoietic. Also called a blood stem cell. They comprise 0.05% to 0.1% of circulating human bone marrow hematopoietic cells.^{1,2} For collection and treatment in this invasive and safe procedure, a cell separator, called the apheresis machine, is used, which in Greek means separation. Apheresis therapy is the removal of one or more components of a person's whole blood. One of the most important steps in the process is the introduction of a sufficient amount of anticoagulant

sufficient to prevent blood components from clotting or clumping together when they are processed through the apheresis device. The anticoagulant flow rate cannot be high, to avoid adverse reactions in the donor/patient. Depending on the amount of anticoagulant returned, you can generate physical symptoms such as tingling in the extremities until the potential damage to the donor/patient.³ The apheresis equipment can be used to remove plasma (plasmapheresis), leukocytes (leukapheresis/lymphocyteapheresis), platelets (thrombocyte-apheresis centre) or the red cells (erythrocyte apheresis).⁴

The apheresis machine performs the separation of peripheral blood and blood products through a technology that utilizes centrifugal effect forces. Cells with higher densities are targeted at specific layers, where they can be identified and collected by a cardiopulmonary bypass induced by the equipment itself. The basic steps of apheresis, are the removal of whole blood from a donor

or patient, separating blood components, plasma retention, or one of its cellular components and returning the remaining elements to the donor or patient.⁵ The principle of operation of this equipment is shown in Figures 1A and 1B.⁶ These centrifugal forces act on only a small portion of the blood, causing the separation of blood elements, called apheresis.

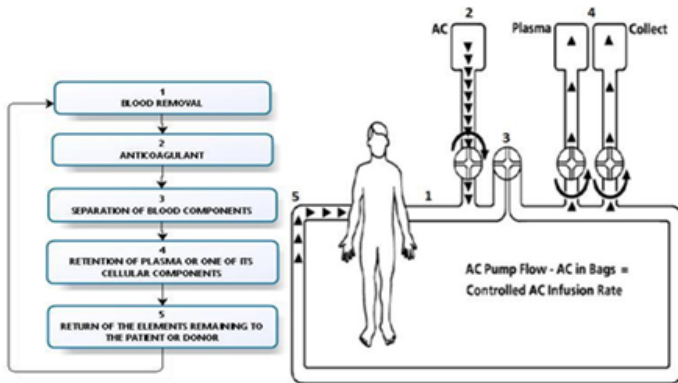


FIGURE 1. Apheresis circuit.

After the end of the cycle, which takes around three to five hours, the desired component is directed into a collection bag. The apheresis machine procedure is initiated by a physician who performs the programming of the parameters based on the mononuclear cells removal-MNC protocol. (The protocol's calculation is based on the amount of hematocrit collected from autologous or allogeneic donor, on the day of the procedure.⁷) The physician keeps up with the process and monitors the physical state of the patient. The physician inputs the age, sex, and weight of the patient or donor and also assesses the need to change the length time or flow rate. At the end of processing, it is possible to collect the plasma cells, platelets, lymphocytes, granulocyte, and erythrocyte as needed. Figure 2 demonstrates the specific blood cell densities.⁸

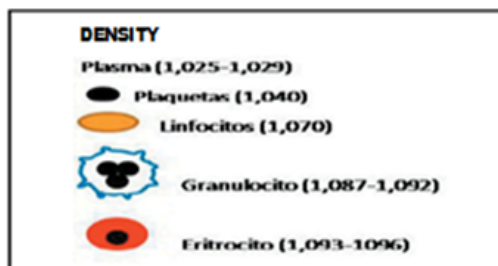


FIGURE 2. Demonstration of specific cell densities.

Considering the given relevance, criticality, and care necessary in the method of separation of cells by apheresis, we need to understand how testing with this equipment is performed. When evaluating the methods of certification effectiveness of operating and the results of the procedure performed by the apheresis machine, it was verified that an item of Brazilian Resolution number 57,⁹ called calibration is not necessarily being performed in a systematized way. This evaluation was done with the manufacturer of the equipment, specialists, and general research. It is critical to confirm the proper functioning of apheresis equipment using calibration, before releasing use throughout the course of its lifecycle. This paper aims to propose and demonstrate a method of accomplishing the qualification of apheresis equipment through calibration, in addition to the usual quantitative testing, before it is released for use.

METHOD

Search

During this process, we checked for quality control regulations for this equipment and standards relevant to its use. It was requested for the equipment manufacturer to provide the operating limits and tolerances of pressure and volume measured parameters as well as procedures to confirm conformity of post-factory output specification. It was verified in article 11 of the Brazilian Resolution 57/2010 that "The Hematology services must have compatible equipment activities and establish a program that includes initial validation, qualification, calibration, preventive and corrective maintenance of equipment and instruments, keeping their schedules and records."

When evaluating the methods of certification effectiveness for operation and results of the machine, it was found that the method used is often a six-month check to compare technical specifications to actual physical parameters. The parameters evaluated are those relating to access pressure, back pressure, pressure leaks, pressure sensors, rotation of centrifugal, circulation pumps, red sensor, and the digital conversion of these parameters.

According to information from the medical care specialists in the subject, normally the form of verification of the performance of the machine is the analysis of

the count of the blood products and blood products of patients, post-procedure. In this case, when the quality of processing is not adequate, there is a need to inform the patient of the need to perform a new procedure and consequently expose themselves again. Figure 3 has the flow method, with job steps.

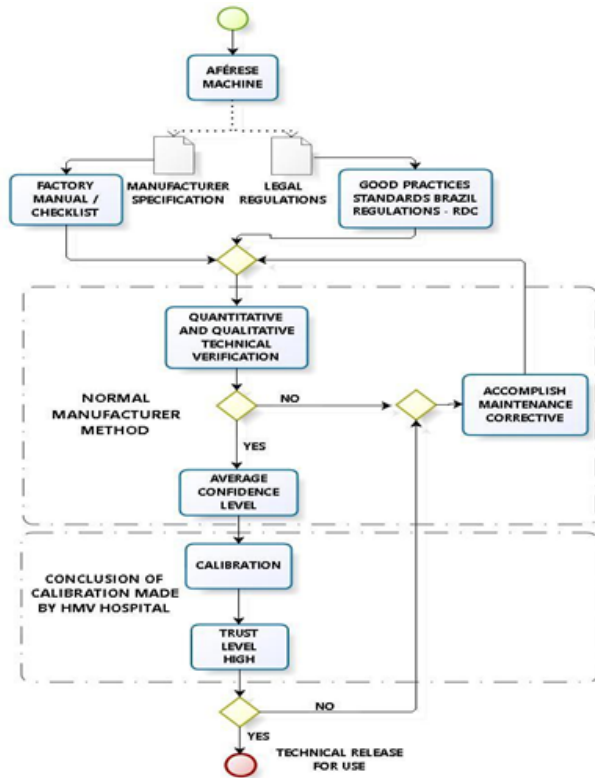


FIGURE 3. The flow method, with job steps.

Figure 3 shows the proposed inclusion of equipment calibration step as a way to raise the level of confidence of apheresis.

RESULTS

Calibration Planning

A qualified company was hired to perform the calibration which evaluated the uncertainties involved and the standard deviations. This was done in conjunction with hospital technicians who assisted in this activity by providing access to the service equipment.

The following parameters were evaluated: pressure (mmHg), back pressure (mmHg), and Protocol MNC in volume (mL). The calibration method for measuring the

volume was to measure the volume by weighing the liquid by time. For pressure measurement was performed compared to the default. The materials used for calibration were: digital scale, digital Timer and Pressure Analyzer.

The calibration results were presented according to the following Table 1.

TABLE 1. Presentation of the Measured Data for the Equipment: a) MNC protocol collection bag, b) access pressure and c) back pressure

a) Apheresis - MNC Protocol - Collection Bag					
Set. Volume (mL)	Value Measured	Average Error	Uncertainty	Total Error	Tolerance Limits
175	179,10	4,10	±0,01	4,11	6%

b) Apheresis - MNC Protocol - Access Pressure					
Set. Pressure (mmHg)	Value Measured	Average Error	Uncertainty	Total Error	Tolerance Limits
- 265	-270,00	-5,00	±0,01	5,01	12%
- 150	-147,10	3,00	±0,01	3,01	12%
- 50	-54,00	-4,00	±0,01	4,01	12%

c) Apheresis - MNC Protocol - Return Pressure					
Set. Pressure (mmHg)	Value Measured	Average Error	Uncertainty	Total Error	Tolerance Limits
52	50,00	-2,00	±0,01	2,01	12%
254	256,00	2,00	±0,01	2,01	12%
403	408,00	5,00	±0,01	5,01	12%

In this way, the calibration procedure was added to the quantitative tests that were conducted for this type of equipment and complemented the proposed qualifying procedure apheresis equipment before release technique to use.

Performing Verification Technician

Among the quantitative tests also performed are: checking the battery voltage of master boards; endurance tests

of the protection earth leakage current; verification of AC and DC voltages; verification and calibration of pressure sensors; functional check of the RBC detector; verification of pump rotation; and simulation with saline.

CONCLUSIONS

Evidence shows that the parameters compared were calibrated within the tolerances stated by the manufacturer. It was noted also that all measurements fell between the variations set and measured (even if within the range of tolerance). In this way, there may be situations where the parameters are very close to the tolerance allowed or even outside of it. Also, we can apply techniques of probability (considering the uncertainties of measurement) to evaluate whether the value measured is within the maximum allowable limit.

Another point to assess is the type of protocols and tests that must be performed in this equipment so that they can reflect, in the most appropriate way, the effectiveness of the process of blood cell separation carried out by the machine.

Considering the details above, there is a need to consolidate criteria and do a greater scope of tests and calibrations on apheresis equipment to avoid initial or routine use of equipment that has not been calibrated. This may help ensure that the equipment performs properly and thus avoid the risk of errors.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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Quality Certification of Medical Devices in Venezuela: Process Developed by Simón Bolívar University, Caracas-Venezuela

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ABSTRACT

Background and Objective: The development of medical technology and advances in biomedical engineering are in constant growth. Every year new medical devices are found in the market that seeks to satisfy the demand and requirements of medical services in health institutions. Consequently, health systems of the countries generate methodologies to regulate and accredit medical devices that really satisfy the needs of medical services with safety, effectiveness, efficiency, and quality. A third party must guarantee the safety and effectiveness of medical technology and issue a quality certification before its available to use in medical establishments. In Venezuela, one of the institutions authorized by the regulatory entity (Ministry of Health) that grants quality certification to medical devices is the Health Technology Management Unit (UGTS in Spanish), attached to the Research and Development Foundation (FUNINDES) of the Simón Bolívar University (USB). The objective of this work is to show the protocol for UGTS certification to comply with ISO 9001 standards and guarantee the quality of the processes of the medical devices certifying unit.

Material and Methods: The process is based on the ISO 9001 standard. Five activities were determined: (i) Prepare the teaching, technical and administrative staff as ISO auditors. (ii) Carry out an external audit, to make proposals for improvement; (iii) Plan changes in our quality management system and processes and qualify as a supplier guided by the ISO 9001 philosophy by a prestigious international company; (iv) Submit our capabilities and to the Ministry of Health, and (v) Execute the protocol to certify medical devices. Medical devices certification includes the analysis not only of the devices itself but the manufacturer, distributor, and post-market services. All these stages and stakeholders are evaluated in the certification process per the guidelines established by the ISO 9001 standard.

Results: The UGTS has developed a protocol that guarantees the safety and effectiveness of new medical devices before its use in the Venezuelan health care system. The protocol is based on the national and international regulations; it has been evaluated by Johnson & Johnson Medical S.C.S. and the UGTS it has been approved as a supplier for the analysis of medical devices by the company in complying with ISO 9001 Standard. Under this new protocol, 550 medical devices have been certified.

Conclusions: Advance on technology allows the breakthrough in medical device development. It is important to acknowledge the need to incorporate less invasive, more accurate and effective devices, in which physicians often rely on to treat a patient, but also developers must be compelled to meet the bioethical principles. The UGTS protocol to certify medical devices is had been recognized and the unit is authorized by the Ministry of Health (MPPS) through the Sanitary Comptroller's Office to issue quality certificates to medical teams since 1999. Approximately 55 companies that have received service are registered in its database. In the period audited (2012 - 2014), 25 files were created. Its processes comply with ISO 9001.

Keywords – *Quality, Certification, Medical Devices, Processes, and Food and Drugs Administration.*

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INTRODUCTION

Medical devices and supplies increase productivity in health institutions, contributing to the reduction of morbidity and mortality rates; however, the use of medical devices has an associated risk. Also, with the advance of technology medical-device complexity had increased over time, representing a challenge to the health system to keep on track.¹⁻³

Currently, there is a great diversity of medical devices, due to the increasing technological and biomedical advances and developments which make it possible to improve the diagnosis and treatment of pathologies, and thus improve the quality and efficiency of medical care services.⁴ Governmental health systems seek mechanisms to regulate the acquisition of these medical devices, to ensure that their use effectively complements quality medical service.

According to the Food and Drugs Administration (FDA), equipment or medical device is Instrument, device, implement, machine, implant, or other similar or related article, including a component, part, or accessory, designed for (1) The use in the diagnosis of a disease or other conditions, or the cure, mitigation, treatment, or prevention of disease in humans or animals; (2) Affecting the structure or any function of the body of humans or animals, without this being done from chemical processes and without depending on human or animal metabolism to obtain the desired result.⁵

The definition presented shows the amplitude of the concept since it includes different teams whose functions vary. Medical equipment can range from a simple thermometer to complex angiography equipment, and both its manufacturing and the complexity of the technology are increasing. A 17.4% growth in employment related to all areas of health including prevention, diagnosis, monitoring, treatment, and care is expected.⁶ Growth will also thrive in the healthcare manufacturing industry.

Internationally it is considered that all equipment or material for use in human medicine should be subject to registration and control by the health authorities of the country of origin to ensure that such equipment or material is "safe and effective."⁷

In Venezuela, the registration and control of medical materials and equipment is regulated by Resolution No.

DM-001 0-99 dated September 21, 1997. Article 1 of the resolution establishes that: "Every juridical person constituted in Venezuela interested in manufacturing, importing, marketing or providing maintenance services of materials and equipment for use at the levels of the health area, must previously register in the National Sanitary Registry that the Directorate of Regulation and Control of Materials, Equipment, Establishments and Health Professions carries out, attached to the General Directorate of Health Controllorship of the Ministry of Popular Power for Health (MPPS).⁸

Article 4 states that: "The materials and equipment used in the area of human health must be registered in the corresponding Directorate of this Ministry contemplated in Article 1 of this Resolution." Among the requirements required to obtain such registration, the interested party must present a Quality Certification issued by an accredited institution (Article 6, paragraph f).⁸

To satisfy this legality, the Venezuelan State has authorized institutions, which have the infrastructure and specialized personnel to guarantee the processes that allow issuing the appropriate certificate, based on the aforementioned principle of "safety and effectiveness." Among these institutions is the Health Technology Management Unit attached to the Research and Development Foundation of the Simón Bolívar University, which is also part of the Biophysics and Bioengineering Group and is an active part of the Biophysics Laboratory.^{8,9}

The safety of medical equipment and material is subject to the criteria of the evaluating specialist and its effectiveness will depend on fulfilling the functions for which it was designed and constructed, according to the manufacturer's technical specifications (that is, that the device does what it says it must do). These two aspects constitute the elements of judgment to issue the quality certificate.⁷

Additionally, any process developed by an organization, to be recognized must have approval of the International Organization for Standardization (ISO). ISO creates documents that provide requirements, specifications, guidelines or features that can be used consistently to ensure that the materials, products, processes, and services are suitable for their purpose.¹⁰

One of the families of the ISO standards is the one called ISO 9001. ISO 9001: 2015 establishes the criteria for a quality management system and is the only standard in the family that can be certified (although this is not a requirement). It can be used by any organization, large or small, regardless of its field of activity. There are more than one million companies and organizations in more than 170 countries certified with ISO 9001.

This standard is based on a series of quality management principles that include a strong focus on the client, the motivation and involvement of top management, the process approach and continuous improvement. The use of ISO 9001: 2015 helps ensure that customers obtain consistent, high-quality products and services, which in turn provide many business benefits.¹¹

The general objective of the work was to show how the UGTS comply with the requirements of the ISO 9001 Standard in the Quality Certification processes for medical devices in Venezuela to guarantee the highest possible quality in each evaluation process of the biomedical technologies that are intended to be commercialized in Venezuelan territory. The specific objectives were: (A) To prepare the teaching, technical and administrative personnel as internal auditors ISO 9001; (B) Request the execution of an external audit, to make proposals for improvement; (C) Plan changes in our quality management system and processes; and (D) Qualify as an ISO 9001 approved supplier by a prestigious international company.

METHODOLOGY

The research performed was a qualitative study, and was exploratory and descriptive according to its purpose.^{12,13} According to its source, the work is documentary. Information was collected from primary and secondary sources. The design of the research is not experimental and from a temporal point of view is longitudinal. Its analysis unit is the process of quality certification of medical equipment implemented by the UGTS-USB. Within the aforementioned process, a series of requirements were identified that must be met for the process to be effective.

RESULTS AND DISCUSSION

Preparation of Staff

The UGTS met with all staff (teaching, technical and administrative) in January 2014 and assumed the commitment over the quality management system as its work philosophy. That same year, two courses were held on this Standard, totaling 112 hours of classes to become "ISO 9001 Auditors." Subsequently, in 2015, the same personnel carried out three courses on ISO 13485 with a duration of 60 hours.

ISO 13485 of Medical Equipment is an internationally recognized quality management system (QMS) for manufacturers of medical equipment and related services. The main objective of the standard is to establish a set of harmonized regulatory requirements for QMSs within the sector of medical devices. It is based on ISO 9001, especially on the requirements of customer satisfaction and continuous improvement, but with modifications to make them more appropriate to the regulatory objective.¹⁴

After Staff Preparation

After the preparation of the UGTS staff an external audit of the certification processes that were being used since 1999 was requested. The audit was carried out by an external university (Metropolitan University) with a School of Production Engineering. Within this university, an expert professor in processes in health institutions was contacted and the field study became degree work for two students.¹⁵

The conclusions of the audit it was found that the Ministry of Health Autonomous Health Comptroller Service does not have specific requirements established for the quality certification of medical equipment so that each accredited institution has freedom regarding the certification process to carry out the evaluation. The requirements recommended by the Food and Drug Administration (FDA)¹⁶ and the Pan American Health Organization (PAHO)¹⁷ were studied. A review of the literature was carried out at the most important universities in Venezuela using the PubMed and LILACS databases and similar works were not obtained. There was no classification of medical equipment according to the level of risk they represent. There was no post-marketing surveillance of medical equipment. Faults were identified in the requirements

related to the technical documentation, specifically related to the capacity of the applicant company to give technical support to the equipment.

Changes in the QMS

To plan the changes in the QMS and its processes several activities were carried out. Once the results of the external audit were known, the UGTS adopted the classification of the FDA's medical equipment¹⁸ and began to request that companies that require the certificate in writing describing their capacity to give technical support for the equipment. The processes were as follows:

- (i.) Company Documentation: Name of the Company; Person to contact; Address and telephone numbers of the company; Technical capacity; List of equipment to be certified with respective technical documentation (catalogs and technical sheets); Estimate of the approximate sale price; Written evidence of technical personnel that will perform after-sales service; Sanitary registry issued by the Ministry of Popular Power for Health of Venezuela. In cases where the company had never been evaluated, we visited its facilities.
- (ii.) Characteristics of the manufacturing company (of the equipment to be evaluated): Name of the Company; Address and telephone numbers of the company; Development areas; Technical capacity.
- (iii.) If the equipment or instruments have a certificate from their country of origin, the most important being those of the FDA (USA), European Conformity (CE) according to Directive 93/68 / EEC, IEC 60601, ISO 13485 and ISO 9001, ISO 62353, the application must be accompanied by the documentation referring to the international certification. Copies of the standards taken as a basis for the issuance of such certificates, as well as of the free sale certificates issued in the country of origin should be included. The required copies must be in Spanish or English and duly legalized by the Consulate or Venezuelan Embassy in the country of origin. In addition, the applicant must issue a letter committing to supply the required material and cancel the invoices for expenses generated during the certification process.
- (iv.) For the issuance of the Certificate by the USB, the equipment must be operational in Venezuela so it can be verified by the specialists in clinical engineering and medicine. If the equipment is not located in Venezuela and the documentation presented meets the requirements, a provisional certificate and a recommendation for its importation will be issued to the respective official body. Once the equipment enters the country and is operational, the technical visit will proceed, and the final certificate will be provided.
- (v.) If the requesting person or company does not have the aforementioned documentation, if the equipment is manufactured locally, or there is a standard for the certification of the equipment and its accessories, the specialists of the USB will proceed with its study to define the protocol or design the set of tests required. The USB will notify the applicant about the materials and equipment that must be supplied to carry out the tests.
- (vi.) If the documents presented are valid, or if it is feasible to initiate the procedures, after a thorough evaluation of its contents and it contains all the sufficient elements required, the certification process will begin, and all interested parties will be notified. If, on the other hand, the documentation submitted does not meet all the requirements required by the Law, or the procedures are not feasible, the pertinent recommendations will be made and all the material will be returned.
- (vii.) After carrying out these steps we will proceed to the analysis and decision-making regarding whether to guarantee or not the quality certificate to the medical team.
- (viii.) After having the new QMS, a working meeting was requested with the Venezuelan Association of Distributors of Medical, Dental, Laboratory and Allied Equipment (AVEDEM),¹⁹ with the objective convey our impressions to our main clients. After the rigorous explanations, AVEDEM remained in agreement as it follows the guidelines of the main specialized agencies in the field.

The process is summarized in Figure 1.

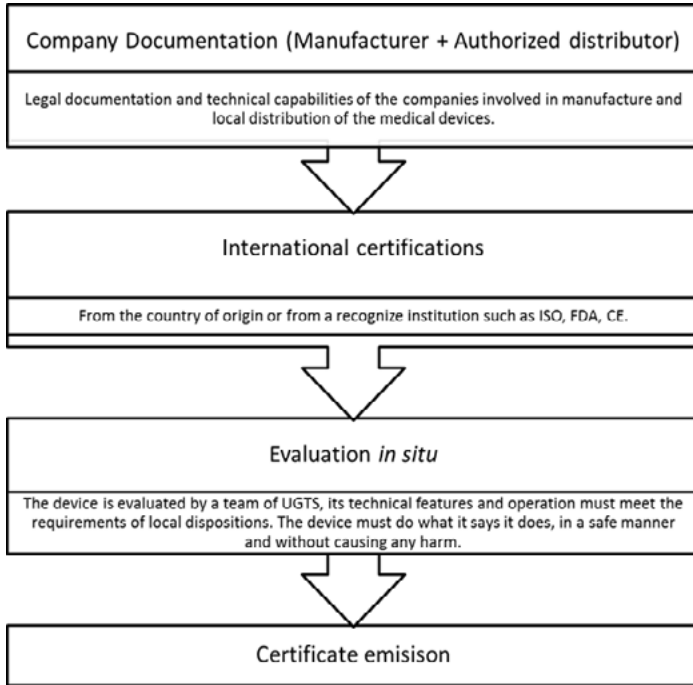


FIGURE 1. Diagram of medical device certification stages. Each stage must be accomplished in order to advance to the next.

Qualifying as a Supplier Under the Performance Standards According to ISO 9001

The prestigious transnational company Johnson & Johnson Medical S.C.S. requested that we in Bogotá (Colombia)²⁰ conduct a remote audit to qualify them as an approved supplier for the certification service of its products in Venezuela. After completion, in January 2017 they were informed that their services were based on the ISO 9001 standard.

Medical Device Certifications

Since 1999 more than 80 companies have requested medical device certifications from the UGTS, for one or more of the devices they manufacture, distribute, and sell in Venezuela. The UGTS have issued certification for over 3000 medical devices since that year. After the incorporation of the ISO 9001 normative to the certification process in 2017, 550 medical devices were certified. These, more recent, certifications correspond to 4 companies with a greater number of devices grouped in families or series. Another aspect that has influenced the certification of medical technologies in Venezuela is the Venezuela-China

cooperation agreement,²¹ signed in 2013 which allows the acquisition, selling, distribution, and commercialization of medical technologies between these countries without the quality certification. Due to this agreement, the presence of Chinese technology in Venezuela, without quality certification, has increased during the past few years.

The most recent 1200 medical devices certified by the UGTS are shown in a graphic form as classified by medical function (Figure 2). It is important to note that this classification is only for this paper as a reference of the certified technological diversity. Figure 2 and Table 1 present the certified devices according to their main function.

Some aesthetic devices that use radiofrequency and

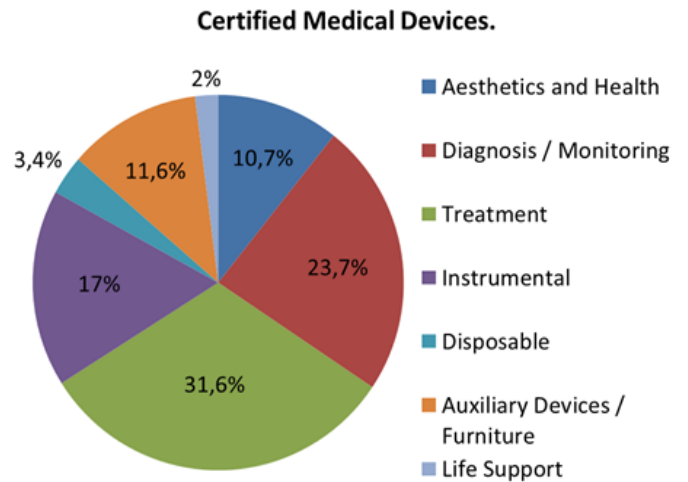


FIGURE 2. Certified medical devices classified by function.

TABLE 1. Certified Medical Devices Classified by Function

Medical Devices Function	Percent (%)	Medical Devices
Aesthetics and Health	10,7	128
Diagnosis / Monitoring	23,7	285
Treatment	31,6	379
Instrumental	17	204
Disposable	3,4	41
Auxiliary Devices / Furniture	11,6	139
Life Support	2	24
TOTAL:	100%	1200

radiation emission are aimed to preserve or restore the health of the skin, as a consequence, they are also considered medical devices. Diagnosis and monitoring

medical devices include those that provide information directly related to pathology and biological variable registries such as electric signals, anatomical images, or metabolites concentration. Treatment and therapy medical devices are those designed to mitigate or eliminate the pathology or condition such as implants, nebulizers, hyperbaric chambers, or infusion pumps. Instrumental medical devices are all metallic reusable tools used during surgeries. Disposable devices are those designed for single-use such as needles, injectors, and condoms. Auxiliaries and furniture are those devices that support a clinical procedure but are not directly in contact with the patient such as centrifuges, plasma extractors, operating room lamps, refrigeration and sterilization equipment, nebulization and oxygen masks, and clinical furniture (tables, clinical beds). Life support devices are those such as mechanical ventilators, anesthesia machines, neonatal cribs, defibrillators, and pacemakers.

CONCLUSIONS

The UGTS is certified by the standard ISO 9001:2015, which guarantees the quality operation of the unit that is authorized by the Ministry of Health through the Sanitary Comptroller's Office to issue quality certificates to medical teams since 1999.

The objective of the certifying UGTS team was to develop the protocols for action and verification, based on the ISO 9001 standard, in the Quality Certification processes for medical devices in Venezuela.

To achieve this goal, the teaching, technical, and administrative staff were prepared as internal ISO 9001 auditors. An external audit was then requested to make proposals for improvement. Based on this audit, changes were made to the QMS and its processes and was immediately made known to the clients. The clients were satisfied, as it follows the guidelines of the main specialized agencies in the field.

Part of the UGTS staff was accredited as ISO 9001:2015 auditors enabling this protocol to be incorporated into the process of medical devices certification. This will guarantee the quality of the management systems of the companies involved in the manufacture, distribution, and post-market servicing of the intended technology.

The importance of certification, as noted by Guberta and Badnjevic¹ and Vukovic et al,²² suggested to the Ministry of Health there was a need for the existence of a clinical engineering unit in every health institution to continuously monitor the performance of medical devices.

Finally, the company Johnson & Johnson Medical S.C.S. requested an audit to qualify them as an approved supplier for the certification service of its products in Venezuela.²⁰ After this was completed in January 2017 we were informed that our services are based on the ISO 9001 standard.²³

Future work is oriented to the automation of the QMS protocol to go along with public policies aimed at paperless transactions at the Ministry of Health.

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Semi-automatic 3-D Reconstruction Measurement of Muscle Volume with Magnetic Resonance Imaging

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ABSTRACT

Background and Objective: We aimed to assess and verify the measurement accuracy and feasibility of semi-automatic magnetic resonance imaging (MRI) volume of interest (VOI) method by comparing its measurements with actual skeletal muscle volumes and discuss the clinical significance.

Material and Methods: A total of 18 muscles from 2 pigs were measured by drainage method, VOI method (V_{VOI}), the summation method (V_{sum}), and maximum section method (V_{max}) respectively after MRI scanning. All measurements were performed by 2 musculoskeletal radiologists and repeated at 6 different times, recording the consuming time (minutes) of every muscle. The average result of the 2 radiologists was adopted.

Results: The 3-D structure of the skeletal muscles was distinct and vivid. A Friedman test and the inter-class correlation coefficient (ICC) indicated the VOI method had a high intra- and inter-reliability. The root mean square error (RMSE) over 6 time-points was 1.101 mL. A Bland-Altman plot represented a superior consistency. Pairwise Mann-Whitney U testing demonstrated that the consuming time to measure each muscle by VOI method was short.

Conclusions: The VOI method could semi-automatically display the 3-D reconstruct of the skeletal muscle clearly, conveniently, with a great accuracy, and high repeatability.

Keywords – *Magnetic Resonance Imaging; Skeletal Muscle; Dimensional Measurement Accuracy; Muscular atrophy; Pigs.*

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INTRODUCTION

Age-related degeneration and some diseases can change skeletal muscle volume,^{1,2} especially in the upper limbs.³ As the volume of muscle determines the maximal muscle force it can generate,⁴ upper limb muscle atrophy can lead to instability of the shoulder joint, causing secondary joint damage, physical disability, persistent arthralgia, and

dysfunction.⁵⁻⁷ The volume of muscle is a predictor of poor outcomes, including mortality, disability, and poor quality of life.⁸ On the other hand, its morphological change is an important indicator for the development of competitive sports training programs, clinical evaluations, and research observation in orthopedics and sports medicine.⁹⁻¹¹ Given

the above, quantifying these features of the upper limb is important for providing context for healthy aging, musculoskeletal disorders, and is a functioning indicator whenever they occur in old or young patients.

Magnetic resonance imaging (MRI) plays an important role in evaluating muscle volume and displaying 3-D structure.¹² Previous studies have reported the MRI 3-D reconstruction and volume measurement by delineating the contour manually.^{4,12-15} However, the manual operation was tedious and less reproducible. In methods such as deformation of a parametric specific object, the mean time for reconstruction was one hour.⁴ It has been reported that the volume of interest (VOI) method, a semi-automatic measurement based on routine MRI, can detect age-related degeneration and rotator cuff tear by measuring the deltoid muscle volume conveniently and directly.¹⁶ However, the accuracy and feasibility of the VOI method had not been verified, especially when its measurements were compared to the actual muscle volumes.

Considering that it is unrealizable to compare the measurements with the actual muscle volumes of the living human body, the ethical problems and limited availability of cadaveric specimens rarely has research on human corpses been reported.¹⁷⁻¹⁹ Nevertheless, an animal model can easily solve the ethical problems and frozen tissue inactivation,²⁰ and swine have proven to be an excellent alternative for practicing and simulating surgical strategies that cannot be performed on human cadavers.^{21,22} Therefore, the primary purpose of this study was to evaluate the accuracy and repeatability of MRI VOI method by comparing the data measured by VOI with the actual forelimbs' muscle volumes of pigs. We hypothesized that the VOI method was accurate and reliable for measuring skeletal muscle volumes, and could provide a convenient and non-invasive way for clinical evaluation of sarcopenia or in orthopedics and sports medicine.

MATERIAL AND METHODS

Experimental Subject

The pig forelimbs for experiment 2 adult middle-aged female domestic pigs were bought from a pig farm where they were reared and slaughtered. The Animal Ethics

Committee was provided with a waiver by our research ethics board. The 2 left forelimbs were transported to our hospital and received an MRI scan immediately after slaughtering. The period between slaughter and MRI scan was approximately 40 minutes. Freshness was maintained at 4° in transportation. We marked these 2 left forelimbs as pig forelimb 1 (PF 1, weight: 3.54Kg) and pig forelimb 2 (PF 2, weight: 3.40Kg).

MRI Scan

MRI procedures were performed with a 3.0T MRI scanner (Ingenia, Philips, Eindhoven, the Netherlands) using an 16-channel Torso Coil. These 2 left forelimbs underwent the standard general clinical MRI protocol at our institution. T1-weighted turbo spin echo (TSE) imaging in the axial: repetition time (TR) = 627.0 ms, echo time (TE) = 20 ms, slice thickness = 3 mm, interlamellar space = 0.3 mm, number of excitations = 1, matrix size = 464 × 459; field of view (FOV) = 240 × 240 (mm), and the acquisition time of this sequence was 6 minutes and 24 seconds.

Drainage Method

After the MRI scanning, the 2 left forelimbs were dissected immediately by 2 orthopedics doctors. Nine muscles were dissected from each skeleton, including extensor carpi radialis/ulnaris (ECR/ECU), extensor digitorum communis (EDC), flexor digitorum profundus caput humeral/ulnare (FDPCH/FDPCU), flexor carpi radialis/ulnaris (FCR/FCU), flexor digitorum superficialis (FDS), and pronator teres (PT)²³ Care was taken to ensure the entire muscle was removed from the skeleton. After dissection, excess connective tissue, tendons and fat were removed from the entire muscle. A total of 18 muscles are shown in Figure 1.

The actual volumes (Vact) of 18 muscles were measured by the drainage method. Figure 2 shows the detailed process. Vact was defined as the actual volume of the muscles. All readings were executed independently and high-resolution photos were taken horizontally by one of the musculoskeletal attending physicians. After the drainage test we checked the results with amplifying photos (Figure 2C), if inconsistent, the ultima Vact of muscle was determined by the high-resolution photos.

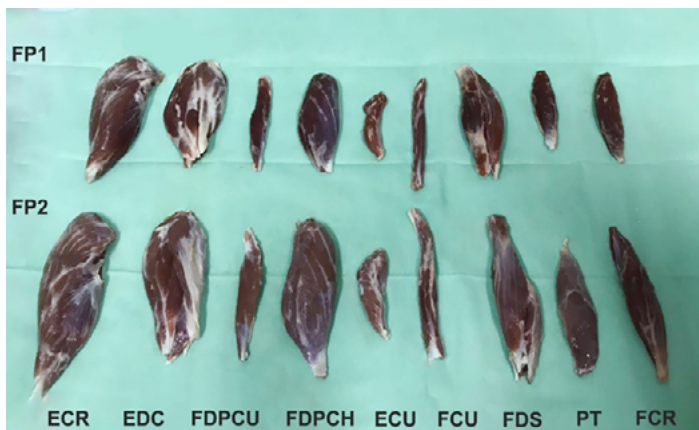


FIGURE 1. A total of 18 muscles were placed on the operating table. The 9 muscles of the PF1 were displayed in the upper row, and the lower row placed the muscles of the PF2.

ECR = extensor carpi radialis; EDC = extensor digitorum communis; ECU = extensor carpi ulnaris; FDPCH = flexor digitorum profundus caput humerale; FDPCU = flexor digitorum profundus caput ulnare; FCU = flexor carpi ulnaris; FDS = flexor digitorum superficialis; FCR = flexor carpi radialis; PT = pronator teres; PF 1 = pig forelimb 1; PF 2 = pig forelimb 2.

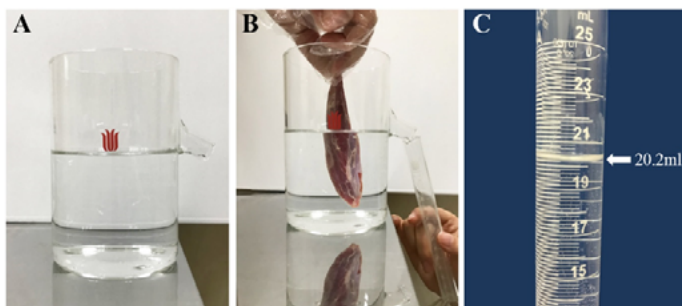


FIGURE 2. **A.** Water was placed in a custom-made cylinder, waiting until the water does not flow out. **B.** The pronator teres was put into the cylinder cautiously and a small-scale graduated cylinder was used to measure the volume of water flowing from the cylinder. **C.** The lowest scale of the crescent was read horizontally and a high-resolution photo was taken to record the scale. The actual volume of pronator teres was 20.2 mm³.

Segmentation Principle of the VOI Method

A semi-automatic method to measure the muscle was applied (VOI method software uMR_770, united imaging healthcare, shanghai, China), which was still investigational. The algorithmic steps of the volume calculating method are presented in a compact form by the following:

a. Given the contours in slices that had been delineated, contours in intermediate slices were calculated using shaped-based interpolation to maintain continuous transition.

1. Calculate the mask from the contour in slices and specify 1 inside the contour, while 0 outside.
2. Convert the mask into a gray-value image through a distance function.²⁴
3. Estimate the contour in intermediate slices by interpolating the distance-representing gray-value slices and thresholding at zero.²⁵

b. A horizontal scan line algorithm is applied to calculate the internal area of the contour. For each scan line:

1. Find the intersections of the scan line with all edges of the polygon.
2. Sort the intersections by increasing x coordinate.
3. Find all pixels between pairs of intersections.

As the calculation of intersections was slow, edge coherence was considered to avoid unnecessary calculation, therefore Active Edge Table was adopted to store active edges related to the current scanline. The contour brings some ambiguity inevitably on whether the pixels should be treated as the interior of the polygon or not. Our criteria are that only pixels whose centers are interior to the polygon are counted. Therefore, the maximum error equals +/- the circumference of the contour multiplied by (largest pixel dimension) 2/2. To raise measurement accuracy, GUI (Graphical User Interface) and images are zoomed in to diminish ambiguousness.

c. The total areas were an accumulation of the areas in each slice. The volume equals the product of the accumulated area and the distance between the 2 slices' center. The volume of a VOI was the product of the spacing (normally the distance between 2 slices' center) and the accumulated area of the VOI projected in each slice.

Image processing by VOI method

The axial T1-weighted TSE images of the 2 left forelimbs were passed to the local workstation, then the VOI method software was performed to reconstruct the skeletal muscle morphology of the pig forelimb and the volume of each muscle was individually measured semi-automatically. One

musculoskeletal attending physician and one musculoskeletal associate chief physician respectively identified every skeletal muscle and contour of the muscle. Only the first/last slice, as well as the slice where the morphogenesis changes need to be delineated manually. The 3-D shape of every muscle was reconstructed and the volume was output automatically. The 2 operators repeated the above image processing 6 times every few days and recorded the entire process time (minutes). The average volume measured by these operators were taken as the result of the VOI method volume (V_{voi}).

Volume Measurement by Conventional Method

Two musculoskeletal physicians measured all the 18 muscles by the conventional method in picture archiving and communication system. The summation method volume (V_{sum}) showed the individual slice volumes, and is shown in Equation 1. The maximum section method volume (V_{max}) was the largest interface to calculate the volume is shown in Equation 2.

$$V_{sum} = \sum_1^n \alpha(l+i) \quad \text{Equation 1}$$

$$V_{max} = \frac{\alpha_{max}(l+i)n\pi}{6} \quad \text{Equation 2}$$

where α was the area per slice, α_{max} was the area of the maximum section, l was the slice thickness, i was the interlamellar space, and n was the number of slices. Repeated measuring 6 times at different times, record the measurements and the consuming time (minutes) of every muscle, adopt the average of the 2 physicians as the result.

Statistical analysis

Measurement data that conforms to a normal distribution were reported as mean \pm standard deviation if not median was adopted. The intra-reliability in different time points were evaluated by Friedman test and inter-class correlation coefficient (ICC) was employed to evaluate the reliability of measurements between the 2 physicians. A Kruskal-Wallis H test was performed to compare the volumes and consume times in different measurement methods. Root mean square error (RMSE) was expressed as the difference between the 3 methods and the actual value. A Bland-Altman plot was applied to the data to display

the distribution of measurements by various methods. A P value < 0.05 was considered statistically significant. Statistical analyses were performed with SPSS software version 21.0 (International Business Machines Corporation, Chicago Illinois, United States) and R program 3.5.0 with calculation of a two-sided P value. All graphics were created using GraphPad Prism version 5.00 for Windows (GraphPad Software, San Diego California, United States).

RESULTS

3-D Reconstruction

The morphological structure and 3-D configuration of pig forelimbs from the reconstruction of MRI VOI method was distinct and vivid (Figure 3), with a high-resolution and was consistent with the known anatomy.

Measurement Repeatability Verification

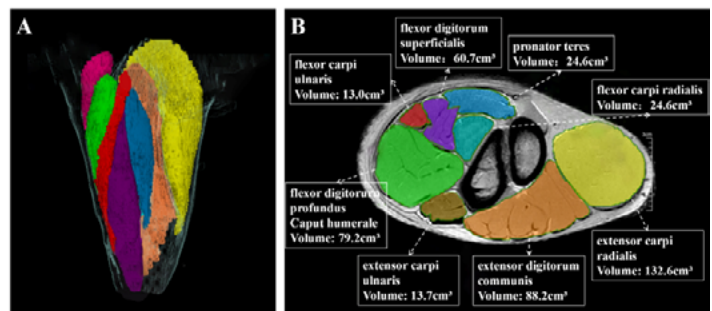


FIGURE 3. A. The morphological structure and 3-D configuration of pig forelimbs from the reconstruction of MRI VOI method was distinct and vivid. B. The cross-section images displayed different muscles using different colors and their volumes showed up automatically.

A total of 18 pig forelimb muscles were measured 6 times by 2 physicians using the MRI VOI method (Table 1 and Table 2). A Friedman test showed the mean rank of all the 6 measurements had no statistical difference ($\chi^2 = 1.396$, $P = 0.925$; $\chi^2 = 9.38$, $P = 0.095$, respectively), so there was a good reproducibility at different time points for one observer. The ICC value calculated from the mean measurement over all time points for each observer was close to 1 (ICC=0.999, 95% CI: 0.998~1.000). The above results indicated that the MRI VOI method demonstrated a high intra- and inter-reliability and good repeatability of volume measurements.

TABLE 1. The Volumes of 18 Muscles Measured Using VOI Method 6 Times By One Musculoskeletal Attending Physician and the Results of a Friedman Test

Muscles	Volumes (PF 1/PF 2, mm ³)						mean	χ^2	P value
	1	2	3	4	5	6			
ECR	123.3/132.6	125.6/130.4	120.8/132.3	125.5/136.5	124.7/134.4	124.9/131.8	124.13/133.0	1.396	0.925
EDC	82.7/88.2	81.5/89.6	84.7/89.2	81.4/92.1	83.8/90.5	80.1/88.4	82.36/89.67		
ECU	12.5/13.7	11.6/13.2	12.3/12.8	13.8/12.84	12.8/13.2	12.9/13.7	12.65/13.24		
FDPCH	63.57/79.2	63.5/78.6	62.4/82.3	66.7/81.4	62.2/83.5	64.8/79.5	63.86/80.75		
FDPCU	12.8/15.2	12.6/15.3	11.5/15.8	12.6/15.0	13.5/14.9	13.7/15.7	12.78/15.32		
FCU	9.5/13	9.8/13.2	10.8/12.4	10.4/13.6	10.6/13.3	10.9/12.9	10.33/13.07		
FDS	65.9/60.7	62.8/59.3	64.6/61.3	66.3/59.4	62.6/59.6	64.2/59.1	64.40/59.90		
FCR	13.8/16.9	14.2/16.4	15.6/16.7	13.8/15.4	15.3/15.9	13.5/15.7	14.36/16.16		
PT	17.7/24.6	18.1/24.7	19.5/24.1	18.7/23.4	19.6/24.3	18.2/25.1	18.63/24.37		

ECR = extensor carpi radialis; EDC = extensor digitorum communis; ECU = extensor carpi ulnaris; FDPCH = flexor digitorum profundus caput humerale; FDPCU = flexor digitorum profundus caput ulnare; FCU = flexor carpi ulnaris; FDS = flexor digitorum superficialis; FCR = flexor carpi radialis; PT = pronator teres; PF 1 = pig forelimb 1; PF 2 = pig forelimb 2.

TABLE 2. The Volumes of 18 Muscles Measured Using VOI Method 6 Times By One Musculoskeletal Associate Chief Physician and the Results of a Friedman Test

Muscles	Volumes (PF 1/PF 2, mm ³)						mean	χ^2	P value
	1	2	3	4	5	6			
ECR	124.6/130.8	125.8/131.6	125.3/135.4	122.7/133.66	125.1/134.5	124.6/134.8	124.96/133.45	9.38	0.095
EDC	84.6/87.6	86.7/88.7	87.2/86.5	86.9/88.4	85.3/88.9	84.6/89.3	85.95/88.23		
ECU	12.6/12.4	12.7/12.7	12.4/10.0	12.3/11.9	11.9/12.4	13.2/11.9	12.53/11.88		
FDPCH	66.2/77.7	65.4/78.3	67.8/79.31	66.9/78.4	64.8/77.3	65.5/78.3	65.92/78.22		
FDPCU	13.7/15.6	14.6/15.3	14.5/16.71	13.8/14.5	14.2/15.8	13.4/16.2	13.95/15.69		
FCU	10.9/12.5	10.6/12.4	10.7/13.55	11.3/11.7	10.8/12.2	10.9/11.9	11.25/12.38		
FDS	61.9/58.3	62.4/58.4	63.2/61.25	62.8/57.3	61.6/57.6	62.4/57.7	62.42/58.43		
FCR	14.8/16.9	15.2/16.8	15.3/15.88	14.7/16.3	15.7/16.5	15.6/16.5	15.28/16.48		
PT	18.5/24.4	19.3/24.6	18.4/22.74	19.2/24.5	18.5/23.8	18.6/24.3	18.93/24.06		

ECR = extensor carpi radialis; EDC = extensor digitorum communis; ECU = extensor carpi ulnaris; FDPCH = flexor digitorum profundus caput humerale; FDPCU = flexor digitorum profundus caput ulnare; FCU = flexor carpi ulnaris; FDS = flexor digitorum superficialis; FCR = flexor carpi radialis; PT = pronator teres; PF 1 = pig forelimb 1; PF 2 = pig forelimb 2.

Comparison of Measurement Accuracy

The volumes of 18 muscles measured by drainage method, MRI VOI method and the other 2 conventional methods were shown in Table 3 (the results were the mean measurement of 6 times by 2 observers). The mean rank

of the 3 methods with Kruskal-Wallis H test were 28.50, 29.06, and 24.94 respectively, χ^2 was 0.724, P value was 0.696, so no statistical difference existed among the 3 methods.

TABLE 3. The Average Volumes of 18 Muscles Measured by Three Methods and Its Actual Value

Volume (mm ³)	PF 1				PF 2			
	V _{act}	V _{VOI}	V _{sum}	V _{max}	V _{act}	V _{VOI}	V _{sum}	V _{max}
ECR	124.0	124.545	125.80	98.91	133.0	133.225	137.23	111.35
EDC	85.0	84.155	83.17	77.27	89.0	88.95	88.96	74.52
ECU	13.0	12.59	12.62	11.34	11.5	12.56	11.12	10.54
FDPCH	65.0	64.89	66.95	63.50	78.0	79.485	78.79	72.26
FDPCU	13.2	13.365	14.13	10.52	15.6	15.505	15.25	14.70
FCU	11.6	10.79	10.56	8.94	10.4	12.725	13.45	10.58
FDS	61.5	63.41	60.98	62.28	57.5	59.165	57.93	53.10
FCR	16.4	14.82	16.43	16.11	16.0	16.32	16.66	12.92
PT	20.2	18.78	20.10	18.25	24.6	24.215	25.14	24.57

ECR = extensor carpi radialis; EDC = extensor digitorum communis; ECU = extensor carpi ulnaris; FDPCH = flexor digitorum profundus caput humerale; FDPCU = flexor digitorum profundus caput ulnare; FCU = flexor carpi ulnaris; FDS = flexor digitorum superficialis; FCR = flexor carpi radialis; PT = pronator teres; PF 1 = pig forelimb 1; PF 2 = pig forelimb 2.

RMSE of 3 methods in 6 time points was 1.101 mL, 1.523 mL, and 8.99 mL respectively. The RMSE between VVOI and Vact was the smallest of all, less than the RMSE of Vsum and Vact or the RMSE of Vmax and Vact. These data showed the VOI method has the highest accuracy

while the maximum section method with the lowest accuracy. Bland-Altman plot represented the minimum bias of -0.2219 between VVOI and Vact (the other 2 were -0.5424 and 5.2162), equivalent to a superior consistency (Figure 4).

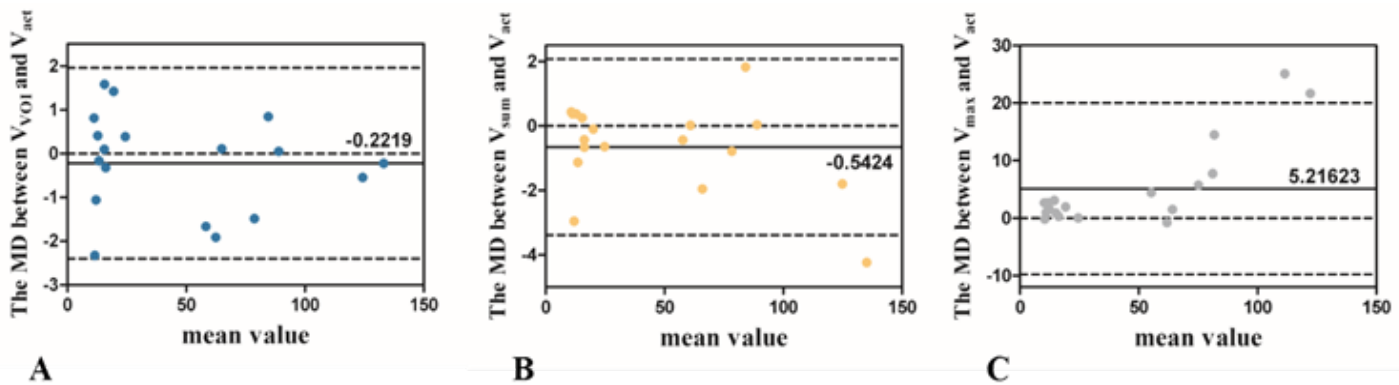


FIGURE 4. A Bland-Altman plot showed a comparison of the consistency of V_{VOI}, V_{sum} and V_{max} to V_{act}. The bias between V_{VOI} and V_{act} was -0.2219, equivalent to a superior consistency.

V_{VOI} = The volume of MRI VOI method; V_{sum} = The volume of the summation method; V_{max} = The volume of the maximum section method; MD = mean value.

Measurement Consumption Time

The median consuming time to measure each muscle by the MRI VOI method, summation method, and the maximum section method was 1.07, 12.68 and 1.25

minutes respectively. The consume time of the 3 methods exhibited significant differences by Kruskal-Wallis H test. Pairwise Mann-Whitney U test and P value adjustment by FDR method exhibited the summation method taken the

longest time ($P = 0.00061$), nevertheless, MRI VOI method and the maximum section method had no statistical difference ($P = 0.2692$).

DISCUSSION

The current examination for evaluating skeletal muscle volumes, includes bioimpedance analysis (BIA), ultrasound, dual-energy x-ray absorptiometry (DXA), computed tomography (CT), and MRI.²⁶⁻³⁰ Nevertheless, MRI has become the optimal method because of its non-invasiveness, high soft-tissue resolution, and 3-D configuration which could observe the morphological structure clearly and animatedly.^{4,31}

In our study, the MRI VOI method was semi-automatic, merely to identify the interesting muscle and contour the enthesis of the muscle and slightly adjusted if the morphology was irregular. The internal slices were measured and delineated by the computer automatically based on the signal intensity, and the organization loss of the internal slices was compensated through interpolation calculation. Its segmentation speed was rapid, and the median consume time to measure each muscle in this study was 1.07 minutes, which was much shorter than the summation method volume (1.07 minutes vs. 12.68 minutes, $P < 0.001$). For another, the pick-up algorithm of VOI method was not only based on the interaction and transformation detecting techniques, but also the visual characteristics. It was seldom influenced by the image noise, so the method could be performed on conventional MRI images and does not require high-resolution scanning, which would have a wider application.

In this study 2 physicians completed the process independently 6 times, the Friedman test and ICC showed a high intra- and inter-reliability, and a good repeatability of volume measurements. What's more, compared with the summation method and the maximum section method, the VOI method has the smallest RMSE, which approximated to the actual values (RMSE of 3 methods was 1.101 mL, 1.523 mL, and 8.99 mL respectively).

The innovation of this research was that the accuracy of VOI method measurements was verified with the true muscle, which was more intuitive and credible. As the morphology and volume of the pig forelimb is similar to

humans, using pig forelimbs in place of intravital human limbs could solve any ethical problems and reduce research costs.¹ In the drainage method, several high-resolution photos were taken horizontally and rechecked by 2 observers (the photos were amplified and viewed repeatedly), which was conducive to collate the readings, ensure the results more veritably, and avoid errors.

This current study has some limitations that should be considered. First, the sample capacity was low. Only 2 left forelimbs (18 skeletal muscles) from 2 live domestic pigs were included in the study, although each method was measured 6 times using 3 methods. Second, although the pig forelimbs were similar in shape and nomenclature to the human upper limbs, there were some differences inevitably. Third, at present the VOI method software was still semi-automatic, in the future, an automatic component analysis through artificial intelligence will be realized, which could reduce the working hours greatly.

CONCLUSION

In summary, the 3-D reconstructs of MRI VOI method semi-automatically was used to display the morphological structure of skeletal muscle. Compared with the real skeletal muscles, the VOI method has been verified to have great accuracy and high repeatability. Herein, this method can be employed as a clinical non-invasive evaluation tool for muscle atrophy such as sarcopenia, age-related degeneration, rotator cuff tears, or be used as an observation indicator in orthopedics and sports medicine.

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A Model for Priority Setting in Health Technology Innovation Policy

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ABSTRACT

Health Technology Assessment focuses on the equal appraisal of health technologies introduced into the market. This has made regulators and the governance of innovation reactive and dependent on the initiatives that innovators take for technology development, thus making it supply-driven. The policy-makers' role has become one of appraising technologies that are already developed rather than guiding the development agenda. This severely limits the possibility to ensure that health technologies sufficiently address major issues such as the burden of disease, trade deficit, and health inequalities. It places governments outside of the actor arena that co-shapes technologies in the early stages, restricting the involvement in facilitating whether to scale up or not. It makes it hard to achieve health technology governance practices that maximally contribute to ensuring technological developments that address public concerns. What is the potential of the framework for changing this dynamic and how can evidence shape technology development agendas without falling into the traps of regulator lock-in or social engineering? The methodology presented in this study takes the first important steps toward an evidence-based framework for priority setting to guide innovations, particularly in the health and social sectors.

Keywords – *Assessment, health technology, medical technology, regulation, innovation, development, priority setting.*

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INTRODUCTION

The appraisal of health technologies introduced in the market is of utmost relevance for healthcare governance. One of the greatest challenges that governments face is aligning the agenda of technology development with social indicators like the burden of disease and macro-economic indicators like trade. However, the role of evidence-based policy restructuring in guiding medical device development has remained an overlooked possibility. Understanding the necessities and gaps in medical device development could have major consequences for sectoral advancement and its benefits to the society instead of being locked in a supply-driven mode. As the current COVID-19 pandemic

painfully shows, it is also necessary to take into account a country's capacity for self-sufficiency in terms of manufacturing the devices used in their territories and becoming more independent from importing medical devices and the economic impacts of such import. The pandemic shows that countries across the world, lower-middle-income countries (LMICs) as well as high-income countries (HICs), have all become largely dependent on the import of medical devices and that self-sufficiency by no means is a concern for emerging economies alone. This study aims to provide an evidence-based framework for priority setting in guiding innovations by developing a practical

model that can be implemented using country-specific data that reflects the actual territorial needs and can be related to the countries' economic capabilities. A set of composite indicators have been identified and used for the priority setting exercise. Firstly, the quality of human life is a major indication of national economic progress and human development index.¹ The corollary of Gross Domestic Productivity as a human health welfare index is an indication of national health,² both economic and contextual. One major parameter for the identification of wellness of populace is public health data records.³ All countries have their specific manner of maintaining public health records⁴ and analysis methodologies⁵ to use evidence from such records.

While minor variations in the analytical tools might be present, one common consensus among all government structured health analytics is the importance of mortality records.⁶ Of the common parameters of assessing disease-affected livelihood, the Quality-Adjusted Life-Year is a generic measure of disease burden, including both the quality and the quantity of life lived. The Institute of Health Metrics and Evaluation (IHME) at the University of Washington published a report titled *WHO Global Burden of Disease (GBD)* which considered Disability-Adjusted-Life-Year (DALY) as the point of consideration for disease-affected livelihood.^{7,8}

To consolidate the data of the major disease burden for India, this study focused on interpolating the diseases that are of immense concern. Each disease has a large number of diagnostic, therapeutic, rehabilitative, and palliative procedures meant for combating the condition. While the diseases are classified under the International Classification of Disease (ICD-11) by WHO, the interventions to tackle such diseases are listed under the International Classification of Health Interventions also by WHO. The interventions are thereafter dependent on various health technologies, and while pharmaceutical products often come with varied alternatives, most medical devices do not have an alternative for the patient nor operationally for the care provider. For example, while several lines of drug therapy exist for non-communicable diseases such as renal failure or diabetes, there are no alternatives to a dialysis machine, a dialyzer, a glucometer, or an insulin pump. There lies an important distinction between

medical devices, with both devices and drugs being health technologies.

Furthermore, by conceptually combining the evidence from the burden of disease estimates for a country to the export-import trade data on medical devices, a model list could be enumerated to estimate which medical devices could be developed in a country, which would be reflective of its health as well as economic impact. This reasoning was applied in this study to India's context. As a country, India currently imports >80% of its medical device needs.⁹ This ranges across all healthcare paradigms as well as all domains of devices.¹⁰ It greatly affects the healthcare cost attributed primarily to capital expenditure on commodities as essential as health technologies.¹¹ The overall medical devices market in India is estimated to be USD 7 billion,¹² however the country imports over 80% of its needs, making medical technology acquisition costlier which negatively impacts the healthcare costs. The medical device market in India is growing at a 15.8% CAGR (compound annual growth rate) and is postulated as the fourth largest potential globally.

The methodology described in this paper, using a model that could cross-pollinate information from both disease burden and trade deficit has several advantages. Firstly, avoidable death or disabilities from disease or ailments that could be possibly cured by medical technology is an effective indicator of meaningful technological and scientific progress. Secondly, the import dependency on such devices including life-saving ones has a direct impact on the country's trade deficit impacting its macro-economic growth and therefore societal progress. Needless to say, United Nations in its 17 Sustainable Development Goals has given equal importance to these by keeping poverty elimination as Goal 1; Good Health and well-being as Goal 3; and Industry, Innovation, and Infrastructure as Goal 9.

Aligning these goals for priority setting in medical technology innovation could, therefore, result in health improvement and economic sustainability. This would also help realign the trade and export-import decision-making processes to encourage domestic manufacturing, which is increasingly important in light of world-wide outbreaks of infectious diseases. To the best of our knowledge, this study presents the first-ever attempt in correlating these

essential principles to establish a pathway for medical technology development and drive innovation policy to improve healthcare access, economic sustainability, and societal impact.

METHODS AND RESULTS

In this section, the creation of a model or methodology to enumerate the priority list of medical devices that need to be developed is explained. The methodology is also a part of the results themselves, given that this study focuses, first, on the creation of a model and then application of the model to do the priority listing. For this reason, the authors opted to merge the methods and the results in the same section.

To estimate disease burden, the main causes of mortality compared over a decade for India, estimated by the IHME was used and are tabulated below (see Table 1). Trends from 2005 to 2015 signify that while there has been a substantial decline in mortality due to neonatal complications, mortality due to metabolic disease and/or lifestyle diseases has overtaken the mortality due to communicable diseases – a classic trend across developing economies.

TABLE 1. Top 10 Causes of Death in 2015 and Percent Change From 2005 (Data from Institute of Health Metrics and Evaluation, India)

Cause of Death	2015 (rank)	2005 (rank)	% change
Ischemic heart diseaseHeart Disease	1	1	(+) 16.7%
Chronic Obstructive Pulmonary Disorder	2	2	(+) 4.3%
Cerebrovascular diseaseDisease	3	3	(+) 7.3%
Lower Respiratory Infection	4	5	(-)(-) 22.6%
Diarrheal diseaseDisease	5	4	(-)(-) 31.7%
Tuberculosis	6	6	(-)(-) 30.7%
Diabetes	7	11	(+) 34.8%
Chronic Kidney Disease	8	10	(+) 20.6%
Neonatal prePre-term birthBirth	9	7	(-)(-) 39.5%
Road injuriesInjuries	10	9	(-)(-) 2.7%
Neonatal encephalopathy	11	8	(-)(-) 31.0%

Table 2 signifies similar parameters in the disability or morbidity estimates since mortality can be indicative but does not singularly affect GDP or macro-economic progress in a population.

TABLE 2. Top 10 Causes of Disability in 2015 (Data from Institute of Health Metrics and Evaluation, India)

2015 Rank	Disability Causes
1	Iron Deficiency Anemia
2	Low Back and Neck Pain
3	Sense Organ Diseases
4	Depressive sDisorders
5	Musculoskeletal Disorders
6	Migraine
7	Skin Diseases
8	Diabetes
9	Anxiety Disorders
10	Chronic Obstructive Pulmonary Disorders

The aspects under study were disease models which required significant medical device intervention, hospitalization, or otherwise. To outline the relevant causative factors and disease conditions, the major disease burdens were classified as communicable and non-communicable. The top five from both were enlisted and relevant treatment procedures that required technological interventions were detailed.

Concomitantly each of the medical devices used for diagnosis and treatment were mapped for each of the therapies corresponding to the diseases. Further, the segmentation of medical devices was charted by bringing in common devices used for these diseases. This had a relationship of one-to-many (e.g., cardiac and pulmonary diseases require more than one medical device) but also of many-to-one (hollow fiber membrane finding application in dialysis, oxygenator, ECMO and the like) (Figure 1).

Table 3 entails the communicable diseases list and technological interventions required to tackle such disease conditions. Table 4 enlists the non-communicable diseases and their diagnostic methods involving technological

interventions that are critical to disease treatment or mitigation.

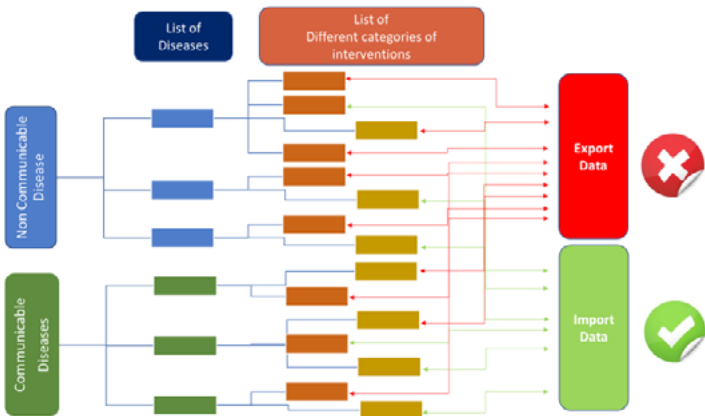


FIGURE 1. Model flow diagram of Burden of Disease to Categories of Interventions to Medical Devices Involved. Starting from the left: (1) Make a list of non-communicable and communicable diseases in order of highest burden (see Tables 1 and 2). (2) Identify diagnosis methods and device-related interventions for the top 5 diseases (see Tables 3 and 4). (3) Create a consolidated list of essential medical technologies (see Table 7) by combining the priority lists of medical and diagnostic devices for communicable and non-communicable diseases (Tables 5 and 6). Next, starting from the right: (4) Tabulate export and import data of categorized medical devices (see Table 8). (5) Consolidate high import and low export-dependent devices (see Table 9) as they require the increase or improvement in internal manufacturing capability to create self-dependency, higher affordability, and greater access.

TABLE 3. Classification of Communicable Diseases and their Corresponding Technological Dependencies

Rank	Communicable Disease or Infectious Disease	Diagnosis Methods and Device-Related Interventionsdevice related interventions and Usesuses
1	Malaria, dengue, parasitic infections like filariasis, and hookworm infestation	Microscopic examination Rapid diagnostic tests Molecular testing Antibody testing (IgG and IgM) Fecal matter testing with PCR assays Endoscopy of intestinal tracts DNA testing Surgery Serological techniques

2	Diarrheal diseases along with amoebiasis and cholera, and similar gastroenteritis, and typhoid	Microscopic examination Cyst search in fecal matter Serological techniques DNA testing Rapid dipstick urine testing Swab samples Laboratory examinations Endoscopy and colonoscopy Blood culture Stool culture Bone marrow culture Widal testing Typhidot medical testing (for detection of IgG and IgM antibodies)
3	Tuberculosis, and fever-associated complications like influenza and leptospirosis	LED microscopic examination Commercial culture and DST Testing TB and drug resistance using Xpert MTB/RIF assay Diagnosis and screening of active tuberculosis in people living with HIV, using lateral flow urine lipoarabinomannan assay Detection of resistance to second-line anti-tuberculosis drugs using molecular line probe assays Diagnosis of pulmonary TB using loop-mediated isothermal amplification Detection of resistance to isoniazid and rifampicin using molecular line probe assays Latent TB infection testing (TST or IGRA) Ultrasound imaging Sputum cultures Mantoux tuberculin skin tests Nucleic acid amplification tests Adenosine deaminase tests Serology, virus isolation and culture, antigen detection, RNA detection by PCR endoscopy Examination using flashlight X-ray Examination using tongue depressors Serum tests Blood tests Kidney function tests Liver function tests ELISA tests PCR tests Microscopic agglutination tests

Rank	Communicable Disease or Infectious Disease	Diagnosis Methods and Device-Related Interventionsdevice related interventions and Usesuses
4	Jaundice and hepatitis, and similar diseases which affects the liver	Blood tests Urine tests Fecal tests LFT Ultrasound imaging Computerized tomography scan Magnetic resonance imaging scan Endoscopic retrograde cholangiopancreatography with the help of X-ray Liver biopsy LFT Hepatitis A, B, D, and C marker tests
5	Venereal diseases like STDs (gonorrhea, syphilis, HIV, etc.,)	Blood tests Urine samples Fluid samples Diaphragm or cervical cap Male condom Female condoms Cervical cap

DST = drug susceptibility testing; HIV = human immunodeficiency virus; LED = light-emitting diode; PCR = polymerase chain reaction; STDs = sexually transmitted diseases; TB = tuberculosis.

Data were collected by taking into account the top five communicable and top five non-communicable diseases which account for the most lives lost as per the latest data available.

With the perspectives of disease paradigm enlisted on priority, our methodology brought in the next component of these diseases and their possible intervention to prevent prevalence or provide treatment. Matching was done between diseases and relevant medical devices of the relevant intervention procedure from the prior lists removing overlapping entities if any. Table 5 lists the priority medical and diagnostic devices in communicable diseases subset, while Table 6 details the priority medical and diagnostic devices list for non-communicable ones. By merging the two previously referred lists and removing overlapping entities, a common list of essential medical technologies was created as shown in Table 7, consolidating this entire dataset. This list is referred to as the “priority list of medical and diagnostic devices on the

TABLE 4. Classification of Non-communicable Diseases and their Corresponding Technological Dependencies

Rank	Non-Communicable Disease	Diagnosis Methods and Device-Related Interventionsdevice related interventions and Usesuses
1	CAD or IHD and their abnormalities	CAD and IHD diagnosis and monitoring using ECG Holter monitoring Event monitoring Cardiac stress testing Ultrasonic imaging of the heart using echocardiography Nuclear stress testing (radioisotopes injected into the bloodstream) Heart CT scan (CT coronary angiogram), which requires high-speed CT scanner Coronary catheterization (diagnosis and interventional purpose, invasive) Intravascular ultrasound Intracoronary optical coherence tomography Fluoroscopy
2	COPD, lower respiratory tract infection, and asthma	Spirometry Chest radiography CT scan Complete blood count Arterial blood gas analysis Other pulmonary function tests
3	Cerebrovascular disease and strokes	Carotid angiogram CT scan Magnetic resonance imaging scan ECG Cerebral angiogram Vertebral angiogram
4	Diabetes and obesity-associated disorders like hypertension	Glycated hemoglobin (A1C) test Random blood sugar test Fasting blood sugar test Oral glucose tolerance test
5	Iron deficiency and protein malnutrition	Complete blood count (using microscope or analyzers) Endoscopy (to check for internal bleeding in the upper gastrointestinal tract) Colonoscopy (to check for internal bleeding in the lower gastrointestinal tract) Ultrasound imaging

CAD = coronary artery disease; CT = computed tomography; COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; IHD = ischemic heart disease.

disease burden context.” This formed half of our dataset for this study.

A second dataset was also created, referred to as the priority list in medical devices from the perspective of trade using export-import data as available in the public

TABLE 5. Priority List of Medical and Diagnostic Devices Communicable Diseases

Communicable Disease	Priority List of Medical Devices
<ul style="list-style-type: none"> Malaria, dengue, parasitic infections like filariasis, and hookworm infestation Diarrheal diseases along with amoebiasis and cholera, and similar gastroenteritis, and typhoid Tuberculosis, and fever-associated complications like influenza and leptospirosis Jaundice and hepatitis, and similar diseases which affect the liver Sexually transmitted diseases (gonorrhea, syphilis, human immunodeficiency virus, etc.) 	<ul style="list-style-type: none"> Microscopes Rapid diagnostic test kits Antibody testing (IgG and IgM) kits Fecal matter examination kits Complete Blood Testing kits (viz. kidney function test, liver function test) DNA and protein-based test assays Devices for serological techniques and Widal tests Kits for biopsy including fluid and tissue Endoscope, Colonoscope, Duodenoscope, and Sigmoidoscope Ultrasound imaging Devices X-ray imaging devices Computed tomography scanner Magnetic resonance imaging scanner Female condom and cervical cap

TABLE 6. Priority List of Medical and Diagnostic Devices Communicable Diseases

Communicable Disease	Priority List of Medical Devices
<ul style="list-style-type: none"> Malaria, dengue, parasitic infections like filariasis, and hookworm infestation Diarrheal diseases along with amoebiasis and cholera, and similar gastroenteritis, and typhoid 	<ul style="list-style-type: none"> Microscopes Rapid diagnostic test kits Antibody testing (IgG and IgM) kits Fecal matter examination kits Complete Blood Testing kits (viz. kidney function test, liver function test) DNA and protein-based test assays

Communicable Disease	Priority List of Medical Devices
<ul style="list-style-type: none"> Tuberculosis, and fever-associated complications like influenza and leptospirosis Jaundice and hepatitis, and similar diseases which affect the liver Sexually transmitted diseases (gonorrhea, syphilis, human immunodeficiency virus, etc.) 	<ul style="list-style-type: none"> Devices for serological techniques and Widal tests Kits for biopsy including fluid and tissue Endoscope, Colonoscope, Duodenoscope, and Sigmoidoscope Ultrasound imaging Devices X-ray imaging devices Computed tomography scanner Magnetic resonance imaging scanner Female condom and cervical cap

CAD = coronary artery disease; CT = computed tomography; COPD = chronic obstructive pulmonary disease; ECG = electrocardiogram; IHD = ischemic heart disease.

TABLE 7. Priority List of Medical and Diagnostic Devices on the Disease Burden Context for both Communicable and Non-communicable Diseases

Priority Common Medical and Diagnostic Devices
Microscopes
Rapid diagnostic test kits
Antibody testing kits (IgG and IgM)
Examination kits for fecal matter
Complete blood tests (viz. kidney function tests, liver function tests)
DNA and protein-based test assays
Serological techniques and Widal tests
Kits for biopsy including fluid and tissue
Endoscope, colonoscope, duodenoscope, and sigmoidoscope
Ultrasound imaging devices and probes (including intravascular ultrasound)
X-ray imaging device
CT scanner (including heart CT scanner)
Magnetic resonance imaging scanner

Priority Common Medical and Diagnostic Devices
• Female condom and cervical cap
• Heart monitoring devices (ECG, Holter monitor, and event monitor)
• Echocardiogram device
• Nuclear stress test (radioisotope)
• C-arm (for cerebral angiogram, vertebral angiogram, carotid angiogram)
• Stents (drug eluting for angioplasty, cerebroangioplasty)
• Balloon catheters (angioplasty, cerebroangioplasty)
• Spirometer
• Mechanical ventilators and accessories
• Nebulizers and accessories
• Disposable resuscitators
• Portable oxygen units
• Automatic insulin pumps
• Syringes with needles
• Sutures and surgical instruments
• Blood bags and accessories
• Portable oxygen concentrators

CT = computed tomography; ECG = electrocardiogram.

domain. This list looked at medical devices apropos their HS codes. The Harmonized Commodity Description and Coding System, also known as the Harmonized System (HS) of tariff nomenclature is an internationally standardized system of names and numbers to classify traded products.

The entire export and import data of categorized medical devices were tabulated as per recent import figures compared against the past few years of export (Table 8). It was postulated that threshold or higher exports indicated self-dependency, higher affordability, and greater access. By opposition, the extreme or high import dependency denoted greater costs and lower accessibility. Figure 2 illustrates the two types of scenarios mentioned, A and B, respectively. The consolidated high import and low

export-dependent devices (driven from the illustrative scenario B) were then highlighted and tabulated into segments that required an increase or improvement in internal manufacturing capability. Table 9 forms the other half of the dataset of the study from the trade perspective.

Further, two of the aforesaid priority lists (Table 5 and Table 9) were overlapped in a Venn diagram format, creating an intersection area of the priority list. The outcome

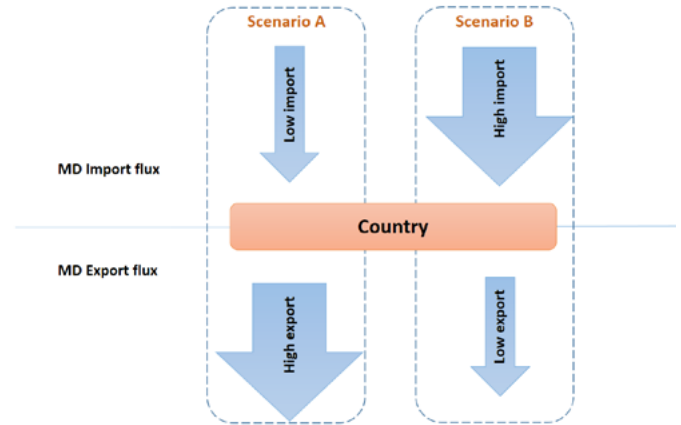


FIGURE 2. Diagram of the import and export data relationship in a country. Scenarios A and B are depicted, as resulting in a lower medical device (MD) cost and higher accessibility (Scenario A) and greater MD device cost and lower affordability. Illustrative scenario B is the focus model of the trade data in this study.

of this entire exercise (Figure 3) was then subjected to expert discussion. The expert group included public health experts, epidemiologists, academia, research scientists, and user specialists.

Using the listed medical devices in the priority list that qualified expert group approval, these medical devices were mapped to their current domestic manufacturing



FIGURE 3. Consolidated modeling of the priority lists from the burden of disease and trade dataset to arrive at the national priority list.

TABLE 8. High Import Category of Medical Devices (Year 2014 – 2015, reference Directorate General of Foreign Trade, Government of India)

S No.	HS Code	Commodity	EXPORT - Year 2013-14 (million USD)	EXPORT - Year 2014-15 (million USD)	IMPORT - Year 2013-14 (million USD)	IMPORT - Year 2014-15 (million USD)
1	90189099	Other surgical instruments and appliances (including veterinary)	59.50	56.08	235.32	246.98
2	90185090	Ophthalmic surgical instrument and appliances	11.09	12.57	117.76	139.15
3	90272000	Chromatographs and electrophoresis instruments	5.03	5.04	104.34	132.97
4	90181990	Other electro - diagnostic apparatus	83.52	68.01	89.84	93.36
5	90181300	Magnetic resonance imaging apparatus	3.23	5.37	74.23	84.48
6	90181290	Other electro - diagnostic apparatus	30.10	83.65	68.31	80.02
7	90213100	Artificial joints	0.68	1.97	63.21	78.50
8	90221200	Computed tomography apparatus	0.52	0.67	70.84	65.03
9	90273010	Spectrometers	1.84	2.52	71.74	59.43
10	90271000	Gas analysis apparatus	4.27	11.00	46.96	58.10
11	90221490	Other X- ray machines for medical uses	84.13	40.14	53.77	52.71
12	90189019	Other diagnostic instruments	17.34	43.94	55.27	51.34
13	90223000	X-ray tubes	20.83	32.78	31.88	43.36
14	90189044	Endoscopes	4.32	6.17	31.14	40.09
15	90184900	Other instruments and appliances, USD in dental science	5.26	5.14	32.80	36.76
16	90189029	Other surgical tools	15.86	12.94	39.35	36.31
17	90221900	Apparatus based on use of x-rays, for other use including radiography/ radiotherapy apparatus	0.86	1.39	32.68	35.70
18	90183100	Syringes, W/N with needles	27.02	30.06	32.92	34.06
19	90183920	Cardiac catheters	1.66	4.22	33.75	32.24
20	30063000	Preparation material for X-ray exams; Diagnostic reagents designed to be administered to patient	8.55	7.96	23.07	23.62

capability. This was named as the Priority List of Health Technology and was used as a key approval criterion by a public agency for providing financial support for further research.

As some devices in the list could have domestic production viability for some of its components but would be completely dependent on exports for other components, it was also critical to understand which critical parts of components needed additional or focused research. To understand the key components of these technologies, two-day technology consultation was organized. This was

named as “FIRST” (Formative Industry Leaders Research Institutes Start-up Partners Technology Meet) to identify essential components for focused research. The technology consultation included innovators, researchers, academia and industry, in which the shortcomings were highlighted and the technology development pathway discussed.

As part of the consultative process, a list of 108 Core Technology Components was identified. The list was then submitted to the concerned agencies within the government that provide funding for technology research. Requests for proposal for these were subsequently released by the

TABLE 9. Priority List of Medical and Diagnostic Devices from a Trade Deficit Perspective

S. No.	HS Code	Medical and Diagnostic Device Category
1.	90272000	Chromatographs and electrophoresis Instruments
2.	90221200	Computed tomography apparatus
3.	90221900	Apparatus based on use of X-rays, for other use including radiography/ radiotherapy apparatus
4.	90273020	Spectrophotometers
5.	90189011	Instrument and apparatus for measuring blood pressure
6.	90183220	Hollow needles for injection, aspiration, biopsy and transfusion
7.	90192010	Oxygen therapy apparatus
8.	90278010	Viscometers
9.	90278030	Instruments and apparatus for measuring the surface or interfacial tension of liquids
10.	30062000	Blood-grouping reagents
11.	90275010	Photometers
12.	90275030	Polarimeters
13.	90189024	Surgical tools, chisels, gauges, elevators, osteotome, craniotomy, bone cutters, etc.
14.	90229020	Radiation generation units
15.	90189033	Hemofiltration instruments
16.	90189097	Nephrostomy/lithotripsy instruments

public funding agency under the categories established as part of Priority List of Medical Devices for Research. The categories include: (1) Biochemistry, (2) Immunology (3) Hematology, (4) Histopathology, (5) Molecular Biology, (6) Genetics, (7) Imaging, (8) Catheters, (9) Ultrasound, (10) Neonatal Equipment, (11) Ventilators, (12) Renal Care, (13) Sutures and Scaffolds, (14) Non-cardiac Implants, (15) Endoscopy, and (16) Muscular dystrophy treatment.

The list elaborates three distinct categories of research priorities.

1. Health Technologies that are not domestically engineered and add to substantial import, high economic costs, and extremely relevant clinical utility.
2. Health Technologies that forms solutions for diseases that have not had solutions globally, such as muscular

dystrophy and their research would be of both national as well as global significance.

3. Health Technologies that focus on disease/clinical conditions reflective of LMICs/specific geographies and whose research would not be priorities in any other geography – such as snake bites.

DISCUSSION

This study aimed to provide an evidence-based framework for priority setting to guide innovation in the healthcare sector. By analyzing a combined dataset of the top ten diseases that account for the most lives lost and trade impact in India, this study specifically developed a method to determine a priority list of medical devices to address both the rising burden of diseases and growing trade deficit in the medical technology sector. Traditionally, the role of policy-makers has been to focus mainly on appraising technologies that are already selected by the innovators for research due to knowledge or engineering capabilities available with the innovators. Therefore, the policy maker's role has been reactive and necessarily not reflective of actual healthcare needs. This methodology allows the policy maker's approach to shifting from being merely reactive to actively driving the agenda of technology development. To do this, it is necessary to find, based on data, what the sectoral needs for development are. To the best of our knowledge, this study is the first to develop a transparent and intuitive method to establish the National Priority List of Medical Devices Research. The results of this study are twofold. Firstly, the formulation of the model can be considered a result in itself. Secondly, the medical device list that resulted from the application of the model/method developed for India is another result.

For the first set of findings, such as the method/model creation, it is important to consider that given its intuitive steps it can easily be adapted to other national settings, for LMIC or even HICs. Similar models could also be applied in other contexts besides the medical device sector, after further testing, like for instance, in agriculture.

In this study, a group of 10 diseases (top five communicable and top five non-communicable diseases) was selected. For other broader studies, this number can also be higher, thus resulting in different scale of results.

Despite the high incidence of communicable diseases, non-communicable diseases account for more than half of the health crisis and are more life-threatening in nature in India.¹³ The comparative weight of the type of diseases (communicable versus non-communicable) could also be taken into account when developing national priorities for research. To the best of the author's knowledge, the only comprehensive study to estimate summary measures of population health for the world, by cause, is the Global Burden of Diseases, Injuries, and Risk Factors (GBD) enterprise, which was updated by WHO for the years 2000 and WHO estimates were subsequently updated for the year 2004.⁷ Later, WHO developed a comprehensive and consistent set of DALY estimates for years 2000–2012 for population, births, all-cause deaths and specific causes of death as well as WHO estimates for some specific diseases and analyses carried out for the Global Burden of Disease 2010 study. Thus, using data on causes of premature death, loss of health and disability in different populations' mortality and disability, other than a disease, would be valuable to enrich the model itself and the resulting list of priority medical devices. Thus, this methodology could be further improved depending upon the contexts and breadth of the application intended.

CONCLUSION

The findings of this study outline extrapolative projections for the future for population health,¹⁴ based on certain demographic and trade assumptions. We use the word assumption with measured responsibility because irrespective of the plausible uncertainty, this is only an application of epidemiological data and its convergence with macro-economic indicators. This is expected to impact a generation of indigenous manufacturing and innovation that are need-driven, market-driven, as well as highly relevant for self-reliance in the context of pandemics. In turn, such innovation policy could guide the government to make strategic resource allocation, positively impact healthcare indicators besides improving manufacturing and employment. Similar models for other sectors/programs that require to be fueled by innovations is suggested for further research.

Governance of innovation has been influenced by very few methods and decision making is reactive to the understanding of technology at the point of product submission. Such proactive methods, one described through this study, could initiate a wider dialogue on resilient innovation policy which has become so much more pressing in times where all nations simultaneously experience enormous dependencies on the import of crucial medical devices.

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Development of a Biomechatronic Device for Motion Analysis Through a RGB-D Camera

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ABSTRACT

This work investigates the validity and reliability of a novel biomechatronic device providing an interactive environment in Augmented Reality (AR) for neuromotor rehabilitation. An RGB-depth camera and telemonitoring/remote alert module are the main components of the device, together with a PC-based interface. The interactive environment, which implements some optimized algorithms of body motion capture and novel methodologies for human body motion analysis, enables neuromotor rehabilitation treatments that are adaptable to the performance and individual characteristics of the patient. The RGB-Depth camera module is implemented through Microsoft Kinect, ORBBEC ZED2K devices; the telemonitoring module for teleassistance and therapy supervision is implemented as a cloud service.

Within the module of body motion tracking, the abduction and adduction movements of the limbs of the full-body structure are tracked and the joints angles are measured in real-time; the most distinctive feature of the tracking module is the control of the trunk and shoulder posture during the exercises performed by the patient. Indeed, the device recognizes an incorrect position of the patient's body that could affect the objective of the exercise being performed. The recognition of an incorrect exercise is associated with the generation of an alert to both the patient and the physician to maximize the effectiveness of the treatment based on the user's potential and to increase the chances of getting better biofeedback.

The experimental tests, which have been carried out by reproducing several neuromotor exercises within the interactive AR environment, show that the feature recognition and extraction, both of joints and segments of the musculoskeletal structure and wrong postures of the patient can achieve good performance in several experimental conditions.

The developed device is a valid tool for patients affected by chronic disability, but it could be extended to neurodegenerative diseases in the early stages. Thanks to the enhanced interactivity in augmented reality (AR), the patient can overcome some difficulties during the interaction with the most common IT tools and technologies; also she/he can perform rehabilitation at home. The physician can also check the therapeutic results while customizing the care pathway in real-time. The enhanced interactivity, provided by the device during rehabilitation sessions, increases the patient's motivation and the continuity of care, as well as supporting low-cost remote assistance and telemedicine which optimizes therapy costs.

The key points of the developed devices are:

1. Making rehabilitation motivating the patient to become an active "player."
2. Optimization of therapy effectiveness and costs.
3. The possibility of low-cost remote assistance and telemedicine.

Keywords – *Body Motion analysis, Smart rehabilitation, Home rehabilitation, Biomechatronic device.*

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INTRODUCTION

Gesture recognition refers to the recognition of significant expressions of a motion made by a person using hands, arms, head, or other parts of the body.¹ This gesture recognition provides a wide range of applications such as:

- Development of aids for the hearing impaired.
- Support for children interacting with computers.
- Monitoring of emotional states or stress levels of patients.
- Navigation and/or interaction in virtual environments.
- Communication in video conferencing.
- Support for patients with specific physical interaction difficulties with machines and computers.

In the last few years, to make more natural and intuitive the environmental interactions with computers new research topics are exploring the direct use of hand gestures, without the use of mouse or joystick, to communicate with machines. The use of controllable interfaces through hand gestures can provide:

- a more natural interaction with the machine since the gestures are a natural form of communication and easy learning;
- a more powerful and effective interaction mediated by the device that acquires both hand position and the trajectories of the extremities of the upper limbs. A single gesture can be acquired by the interface to identify both a target object and the action to perform on it; and
- direct interaction from a cognitive point of view where the hand becomes the input device, without needing to intermediate transducers.

Some studies on the use of gestures for human communication have detected that 70– 80% of verbal messages during a dialog may be expressed exclusively through gestures that involve all parts of the body.²

Systems that exploit interactions mediated by gesture-recognition technologies can also provide a valuable tool for people with limited motor skills by allowing an efficient human-machine interaction based on a limited set of gestures or body movements. AR could also return to prominence by becoming a promising form of investment in military, entertainment and medical industries.

Especially in clinical rehabilitation, AR can improve the experience of patients by increasing the effectiveness of treatment.³

The main feature of AR systems is the ability to adapt the experience of a patient to his real physical ability.⁴ Furthermore, the arrangement of the joints and the measured value of joint angles must be taken into account. This allows the patient to objectively assess the effectiveness of treatment with the possibility of increasing the biofeedback.⁵ The real-time monitoring and measurement of the user's performance can provide biofeedback and, consequently, also aid in the evaluation of improvements or deterioration of the patient's performance. The evaluation of the performance can be achieved based on some performance indices and clinical protocols see.⁴

There is evidence that most patients can benefit from virtual reality rehabilitation. This includes patients who have had strokes,⁵ patients who need to recover limb motor skills in general,⁶ patients who need to perform neurorehabilitation in the early stages of recovery,⁷ as well as the elderly, children, and anyone who needs to work on posture or balance.⁴

This study aims to develop and test a rehabilitation device that motivates the patient to become a "player," by optimizing both the effectiveness and costs and provides the possibility of implementing, in a clinical and/or domestic context, low-cost and remote assistance and telemedicine services.

The current study is part of a more complex project that takes into account the following main steps:

Step-1: Identification and preliminary testing of different commercial devices using the RGB-D camera for rehabilitation purposes and analyzing different rehabilitation scenarios to conceptually represent the entire rehabilitation process.

Step-2: Building the first prototype using commercial hardware and implementation of dedicated software for image acquisition and processing.

Step-3: Testing of the prototype and the software in a simulated but real context. At this point, all the components of the device are globally tested and compared to standard clinical practice (process and tools).

Step-4: The rehabilitation protocol implemented is extended into the prototype.

Step-5: The system moved to the experimental stage and was tested on large scale involving different clinical partners to produce data for assessment of the device performance, not just on hardware but considers the whole process of rehabilitation mediated by the biomechatronic device.

Currently, we are working on the Step-3 of the project and this paper describes the experimental results obtained on the performance during the interaction of the patient-biomechatronic device within the AR environment.

MATERIALS AND METHODS

Body motion capture and motion analysis in an environment for interaction in AR is based on the use of a RGB-Depth camera (Microsoft Kinect) and video output devices (PC monitor or projector); the interaction environment is conceived to support adaptive and customized neuromotor rehabilitation during some exercises that promote the interaction between the patient and the device.

The system, as shown in Figure 1, can be divided into 3 distinct macrophases: (1) A phase of pre-processing carried out on each captured frame, which allows to segment one or more human figures; (2) A conversion phase that allows converting the obtained image into a segmented model, functional to the next step and achieved at low computational burden required for the extraction of the points in order to track the different parts of the body (arms, legs, and head); (3) A post-processing phase that allows the extraction of the movement.

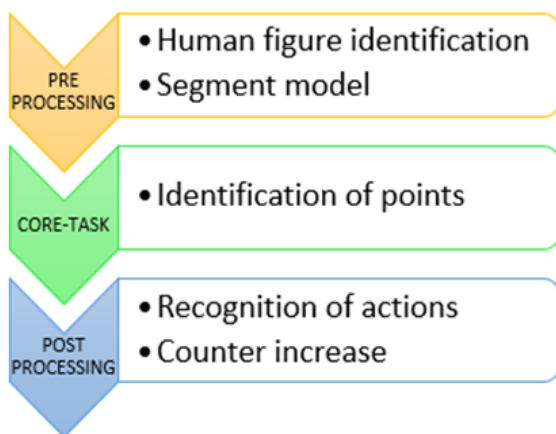


FIGURE 1. Main phases of the system.

The flow diagram shown in Figure 2 summarizes the steps point by point. Steps 1, 2, 3, and 4 are made by recalling the Microsoft's Kinect for Windows SDK functions, while the following steps (5, 6, and 7) have been developed specifically for the functions made available in Processing, a real open-source programming language that has enabled the acquisition and the elaboration of the data stream from Microsoft Kinect and other compatible devices.

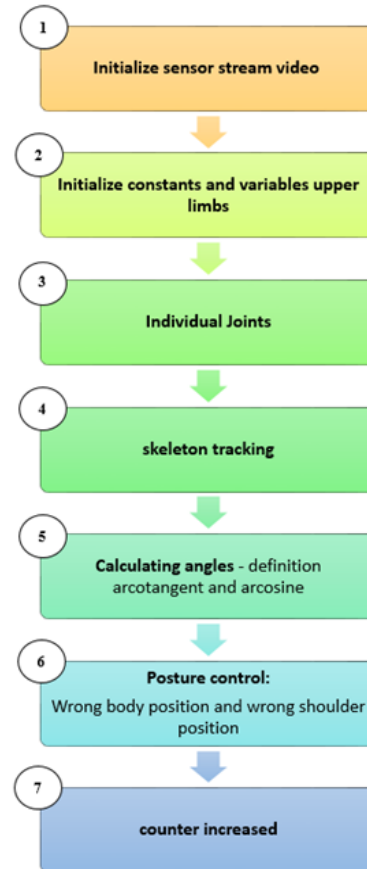


FIGURE 2. Flow diagram of the algorithm used to process the patient data during the rehabilitation session.

The presentation and the discussion of the results obtained for the rehabilitation of the upper limb are discussed in the next sections. The main features of the device are (1) tracking of the body, (2) calculation of detected angles; (3) posture control, and (4) performance acquisition.

1. The basic algorithm can able to identify the body joints and to track their position. The tracked movements of abduction and adduction of the upper limbs are visualized in real-time and in AR and the visual support to the patient improves the execution of movements and the patient's performance.
2. The calculation of the joint angle detected on the tracked limbs during in the different opening and closing positions and the visualization of the values of the angular displacements are carried out in real-time. In this step, the variables and constants are initialized for the right and left upper limbs.
3. Posture control during the exercise execution is determined by 2 methods "Shoulder Check" and "Body Check."
4. The device starts to acquire the patient's performance and then checks the correct posture at a constant acquisition rate during the rehabilitation session. Finally, the output is stored and transferred to the cloud service.

To develop our rehabilitation prototype, we used a Microsoft Kinect. It consists of an RGB camera with a resolution of 640×480 pixels to 1280×1080 at 30 Hz that can be increased at the expense of a drop in frame-rate. The same device is equipped with a depth camera consisting of an infrared projector and a monochrome CMOS camera with a resolution of 320×240 pixels. Finally, an array of 4 microphones for listening to voice commands is integrated into the Microsoft Kinect. For both cameras, the viewing angle is 57.5 degrees in horizontal line and 43.5 degrees vertically, with the possibility of extending the last one by 54 degrees thanks to the inclination platform that is equipped with a motor that rotates the sensor to automatically center the user.

Other features are 3 optical devices for visual recognition of the moving body, 2 video cameras and an additional infrared sensor, and a Kionix KXSD9 three-axis accelerometer.⁸

Each patient is analyzed separately. This choice allows the focus to be on the blob of each patient that can be extracted from the background. In the developed model, the main steps of the proposed system have been identified as solutions to the following problems listed below.

- What technique is adopted for segmenting the human figure?
- Which parts of the body are recognized and the related movements to be tracked, with low computation burden, by optimizing the precision/performance ratio of the recognition and tracking algorithm implemented into the device?

Once the above problems are solved, the selection and the development of the algorithms for detection and tracking of the target movements of the body have been performed.

The identification of the points of the body segments as target features, which are important to describe an action and to track body motion, takes into account all the points of the image and provides an estimate of all points in the form of a "line" according to the following 5 variables below.

1. The expected position of the patient (for example standup).
2. What point is detected and its anatomical name.
3. The environmental characteristics of the scene such as the illumination level of the room.
4. The patient's position is centered into the scene.
5. The Cartesian coordinates of the joints of the tracked musculoskeletal structure.

For the study of movement, the approach used is based on an algorithm that calculates the opening angle of the upper limb. After the identification of the skeletal segments and joints, the next step is to calculate the joint angles of the musculoskeletal structure from the Cartesian coordinates extracted from the segmentation image data.

After presenting the principles functional features of the rehabilitation system and before evaluating the motion tracking performance, the approach taken for implementing the overall system, made by the user interface and body motion analysis module, is presented here.

Since the software is intended for a target group of patients with motor problems but also for a target group that is halfway between rehabilitation and neurodegenerative diseases, the model developed was designed to be as intuitive and easily manageable as possible. The

font size of the text was chosen according to the reading from a certain distance and red was the color chosen to make it immediately visible to the patient.

First of all, we note the division of the rehabilitation interface into 2 areas regarding the exercises to be performed with the right arm (top right), with the left arm (top left). Also, for each limb, the visual output of the detected angle is given.

In the middle of the window, the mirror image of the patient detecting depth is displayed on the screen in real-time. The mirror image allows the patient to better coordinate body movement and also to identify the target joints and segments of the skeletal structure on which the therapy is focused. Once the recognition by the Kinect has been performed, a sequence of segments and a series of ellipses in a yellow, red, green, or blue color is used to highlight the joint junctions.

The procedure that allows us to understand where the joints inside the human skeleton are located is called pose recognition in parts, and it is realized starting from the depth image. The approach used refers to modern and robust techniques in object recognition based on the principle of subdivision of objects into parts.

The Kinect obtains 3-D information from the analyzed scene by creating a depth map within it. This map is normally obtained through a stereovision system but the Kinect is not such a system as it is equipped only with a color camera, a depth camera, and an infrared emitter.⁹⁻¹⁰ The solution adopted was that the infrared emitter projects a large number of light spots into the environment whose distribution, at first sight, seems random. The emitted pattern is visible by turning off the lights and framing the environment with a digital camera.

The optical sensors contribute by providing the PrimeSense PS1080-A2 chip with the necessary data to create an image containing depth information related to the observed scene. This image also contains a certain amount of information related to the distortion of the spots with respect to their ideal position. In this way, the Kinect determines the distance of the objects in the scene and their conformation.

After recording a depth image of the observed scene, the next step of the process involves the software execution of the tracking algorithm that identifies the number, the position, and the skeletal joints of the human skeletal structure that are to be tracked.

Microsoft's tracking algorithm¹¹ is the result of 500,000 samples of recorded data concerning different human behaviors (dancing, moving, greeting, etc.). The tracking data is processed in real-time and provided to the computer where the Microsoft Kinect is interfaced. A result of this tracking is the skeleton data will be available as a Skeleton object, obtained by calling the `getSkeleton()` function. The position and orientation of each articulation are stored into the SkeletonJoint object, which can also be obtained by using the `Skeleton.getJoint()` function. To obtain information about the various joints, such as position and speed, to measuring user attention, or to draw the skeletal model (joints), is it possible to use the function `JointType joint = user.getSkeleton().getJoint(JointType.(anatomical part of interest))` which will return an object of JointType type giving information about the target joint.

This provides a general method for the representation of open kinematic chains, and the attachment of reference systems to the joints to determine their characteristic parameters as shown in Figure 3.

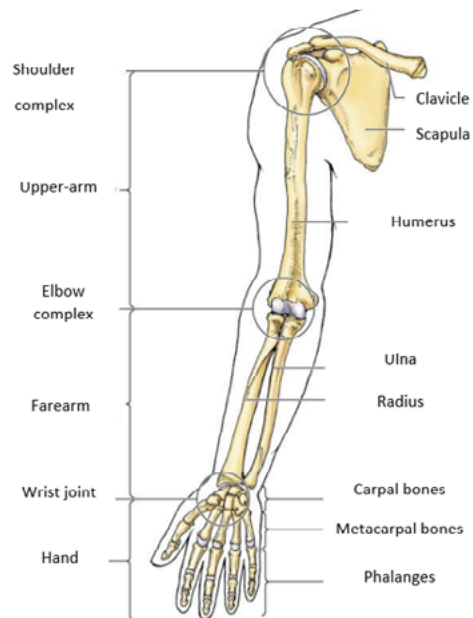


FIGURE 3. Arm joints used for the kinematic model.

Once defined the reference systems and assigns constants representing the lengths of the various links:

- A) the length of the shoulder
- B) the length of the arm
- C) the length of the forearm

Detection of the Position of the Arm Joints

While previous problems are more theoretical, the first practical problem concerns the angles measuring the arm joints and then the data output for the display device and remote monitoring. To solve this problem, we reference the joints J1 and J2 as shown in Figure 4.

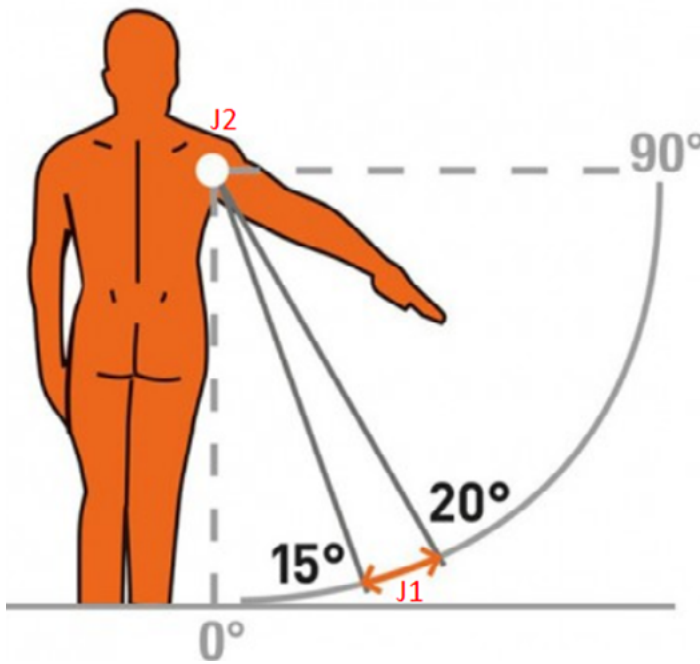


FIGURE 4. Variation of the angle in the abduction-adduction movements.

To calculate the angles of the arm joints, the position in the Cartesian space of the joint are taken from the image data stream. We consider 3 basic elements of the arm (shoulder, elbow, and wrist) to obtain the tracked angles.

The calculation of these 2 angles of the shoulder and elbow is based on trigonometric transformations (atan and asin functions) from the position in the Cartesian space of the joints identified by the tracking module.

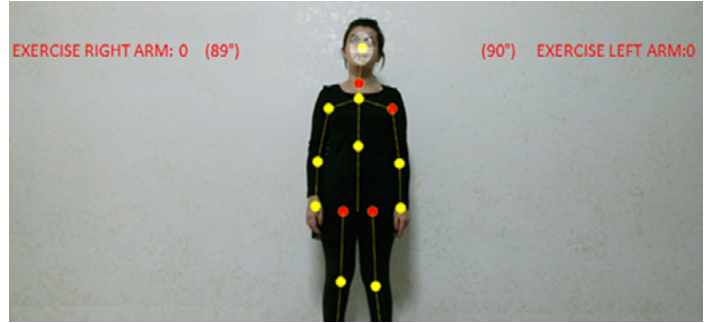


FIGURE 5. The image shows the initial values of the patient.

To calculate the angles of the various arm joints, a count_step method has been developed that uses the Kinect libraries to detect the position in Cartesian space of the 3 fundamental elements of the arm (shoulder, elbow, and wrist) and then algebraically obtain the angles.

From the trigonometric projection of Figure 6, the angles are derived from the position in Cartesian space of the points identified by Microsoft Kinect device.

```
Float m1=0;
Float m2=0;
Float P1X = joints[jointType1].getX();
Float P2X = joints[jointType2].getX();
Float P1Y = joints[jointType1].getY();
Float P2Y = joints[jointType2].getY();
m1 = (P1X-P2X);
m2 = (P1Y-P2Y);
Int A1= (int) Math.abs(((Math.atan(m2/m1))*100 / Math.PI));
```

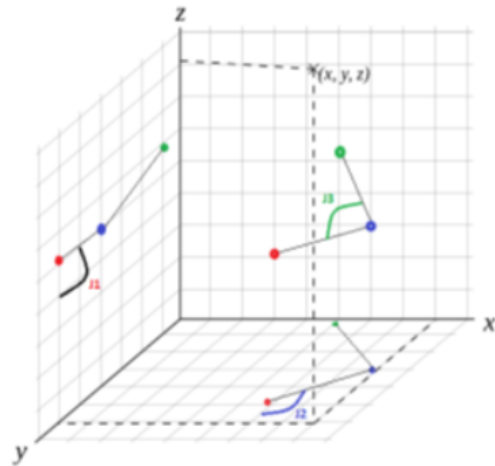


FIGURE 6. Projection and angle calculation.

The algorithm involves the calculation of the arguments of the atan function in terms of the increments m_1 and m_2 along x-axis and y-axis respectively. The values of the Cartesian coordinates of the 2 joints on the same musculoskeletal segments are used to calculate the angle. The results show the device can measure a joint angle with a margin of error of $\pm 1^\circ$. The margin error has been estimated by comparison with a set of repeated measurements performed on the shoulder through a set of protractors commonly used by physiotherapists.

The experimental tests have shown that the system is also capable of checking the patient's correct posture. An alert is generated if the patient's shoulders or body are in an incorrect position, by taking also into account a threshold interval such as around a reference angle of 0° achieved by the shoulder during the horizontal position of the upper arm. The device displays a warning on the AR interface by giving the patient information about the type and side of the wrong position. The same information is transmitted by email to the therapist at the end of the session by the telemonitoring module through a report collecting the number and types of the patient's errors. If the subject's position is incorrect, performance will be paused until the subject resumes the correct posture to perform the exercise. Examples of wrong positions detected are shown in Figure 7 and Figure 8.



FIGURE 7. Wrong position detection for right shoulder.



FIGURE 8. Wrong position detection for body.

RESULTS

The device performance has been tested in:

- a controlled environment with only people who want to interact with the system present in the field of view of the webcam;
- a heterogeneous background for each test performed where the background has heterogeneous characteristics (shades, shadows); and
- short distances where the distance between the patient and the location of the webcam (and screen) does not exceed 3 meters.

During the tests performed during rehabilitation sessions on the upper limbs, the points that identify the joint junctions are almost always detected correctly, obtaining good accuracy. The device uses a detection algorithm of a wrong posture during rehabilitation sessions. The algorithm has taken into account 2 reference points for the body and the shoulder, and calculate a gradient. If the slope is greater than a threshold, the device does not consider the wrong exercise. Table 1 shows the values measured in a patient session.

TABLE 1. Values Measured in a Patient Session

	Starting angle	End angle
Right arm	76°	2°
Left arm	80°	5°

ABDUCTION-ADDUCTION OF THE RIGHT AND LEFT ARMS

The movement starts with the arm in the rest position and the counter is increased only when the arm is at 90° relevant to the bust and returns to the initial position. If the patient performs the movement "by half," meaning it reaches an opening lower than the established ones, the counter is not increased.

The actual repetition count only occurs if the patient completes the movement such as if he starts from a rest position, performs abduction, until he reaches 90° position, and then it returns to the rest position through the adduction of the arm (Figure 9). Since the system has

tolerance thresholds of $\pm 1\%$, the count is considered valid if the measured value falls within this threshold.

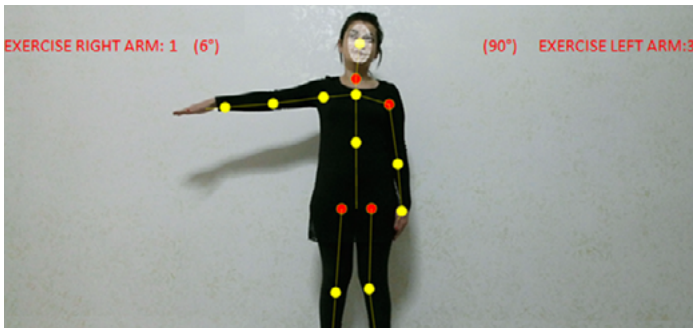


FIGURE 9. Counter increase. Movement begins with the arm in the rest position, the counter is increased only when the arm is J1/J2.

SHOULDER REHABILITATION RESULTS

The proposed isotonic exercises aim to recover joint mobility and optimize joint function. The goal of the execution of the exercise, from 0° to 60° , is to restore a normal joint function with an opening angle up to 180° .

After this first evaluation, related to the movements of the trunk (and therefore the pelvis), the patient's hands were placed along the axis of the trunk. The patient was then asked to tilt their torso. The test was successful and just as expected, when the tilting exceeded the permitted tolerance limit, the patient was notified of the incorrect position of the trunk.

The results obtained and the sequence of exercises used in the rehabilitation path, with reference to the rehabilitation standards taken as a reference,¹² show that the values obtained compared to those measured in normal clinical practice and are more than satisfactory.

The device is also equipped with a telemonitoring module that is connected to the cloud and can send the patient's performance to the physician (or physiotherapist) in real-time. Thanks to the telemonitoring system, the physician can optimize the rehabilitation path according to the patient's performance.

DISCUSSION

From the experimental findings it possible to conclude that the exercises mediated by the AR interface can effectively support the main rehabilitation protocols both

for the recovery of mobility following trauma and for the case of surgery.

In shoulder rehabilitation protocols, in the case of surgery involving the rotator cuff, or even in the case of surgery for proximal fractures (near the shoulder) of the humerus, isotonic exercises (including abduction and adduction of the arm), must be performed standing in front of a mirror, taking care not to contract the upper beam of the trapezius muscle, that is, avoiding the elevation of the shoulder. The objective is to recover joint mobility and to optimize joint function; the exercise is performed from 0° to 60° , until the joint function is reached that allows an opening up to 180° .

It is emphasized that the movement during the exercise should be performed slowly and should not be painful and the exercises should be avoided if the joint is sore or swollen, since the rehabilitation session not only aims to strengthen the muscles but also increase the amplitude of the joint movement, while improving the precision and safety of the movement.

It is also useful to perform the exercises with the joint that not affected. As shown by the results obtained, the system can be easily integrated into standard clinical practice and, at the same time, the device easily customizable to guarantee, personalized rehabilitation-functional path.

CONCLUSIONS

In this study, the Microsoft Kinect V2 has been tested by assessing the performance of the motion tracking of a patient in rehabilitation. The experimental tests show that the tracking algorithm implemented is very robust and the system performance has been characterized over several operating conditions. The estimated accuracy during tracking is a few millimeters in most cases. The tracking algorithm follows the full-body figure of the individual as long as they remain within the field of vision of the RGB-D camera. The tracking performance is strongly affected by the following circumstances: a limb covering another one, an object placed into the scene, and a camera point of view not perpendicular to the frontal plane of the body. In these cases, the visualization of the tracked trajectories and body elements into the virtual reality scene was affected by some drift between the 3-D

visualization and the real points on the patient's musculoskeletal system. Accuracy is the main requirement needed evaluate the sensor performance as objective as possible after considering all the performance constraints involved in the rehabilitation tasks used for testing the device. In this respect, the achieved maximum accuracy of 1° is satisfactory.

At the current development stage, the estimation of system performance has been carried out by evaluating the tracking accuracy of the joint angles from 0–90°. The accuracy is measured as the angle of error between the output of the mechatronic device and the protractor measurements carried out manually on the patient during abduction–adduction exercises.

In conclusion, the strong points of the device and resulting rehabilitation model are its accessibility and usability. Following the preliminary phase of definition of the design constraints based on the needs of standard rehabilitation protocol, the obtained results are the design, testing of a device, and the assessment of its therapeutic applicability that support an intuitive interaction together with the adaptation to the specific performance and individual characteristics of the "target" user.

The device provides a valid tool for people with chronic disabilities but also for the treatment of neurodegenerative diseases, especially in the early stages. Thanks to the conceived interactive model, patients can improve their quality of life by overcoming difficulties in interacting with the most common digital tools and new technologies (information technology) that can be introduced in healthcare facilities as well as in everyday environments, to improve therapeutic performance and optimize cost.

Therefore, patients can carry out the rehabilitation exercise sessions independently but at the same time they can be supported and encouraged and, above all, the physiotherapist can "control" the results in real-time, allowing a better evaluation of the evolution of the treatment path together with greater personalization and higher frequency of treated patients over time providing the advantages of low-cost teleassistance and telemedicine in the context of "at-home rehabilitation,"

As a further development of the device, a voice recognition module will be implemented, as the voice signal can

be used to start the rehabilitation session or to interrupt and then resume the exercise later. Another important development concerns facial recognition. The ability to customize the "list" of exercises that the patient has to perform and the extension of the dataset of exercises made available to the patient would be most useful. This could expand the possibility of therapy and to make the rehabilitation model more complete and effective.

At the current stage of the development, we are testing the use of hardware platforms, like the Kinect (Azure, Orbec 3D), that support the Processing software. By exploiting the enormous progress in the field of machine learning, further tests are being addressed through the use of a normal web camera for tracking movements that at present; however, it still guarantees a suboptimal accuracy compared to those obtained in this study.

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Bedside Communication and Management of Vital Parameters and Alarms In Care-Intensive Environments: Simulation Model Development for the Clinical Effectiveness Analysis of an Innovative Technology

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ABSTRACT

Background and Objective: The deliberation n.7301 of 31/12/2001 provides for the inclusion of a call system with acoustic and luminous signaling within the minimum equipment of the recovery ward. However, traditional call systems are inefficient since they are based on the following incorrect assumptions: patients and staff are unmoving, information sources are static, and assistance is unidirectional. Taking care of a patient involves different personnel who should be dynamic and should be able to exchange information. Furthermore, the high number of clinical calls and alarms might be an issue, as they are essential to fulfill patients' needs, but could cause stress and additional workload for medical staff. Indeed, they sometimes ignore some calls or waste time on non-urgent requests. Also, the identification of an alarm and prompt intervention seems to be more difficult during travel. An ideal alarm system should have 100% sensitivity and specificity. However, the alarms are designed to be extremely sensitive, at the expense of specificity. The *alarm fatigue*, that is the work overload due to an excessive alarms number exposition, is a critical problem in terms of safety in the current clinical practice because it involves desensitization and alarm loss, and occasionally a patient's death.

Material and Methods: Appropriate approaches to notifications should be evaluated, including the effectiveness of mobile wireless technologies that are key to linking patients, staff, data, services, and medical devices which simplifies communications and workflows. Several issues related to the communication among staff members, between patient and caregiver, and regarding the alarms and vital parameters distribution in care-intensive environments have been analyzed. The focus was on the clinical effectiveness analysis of innovative technology to support the activities in the Emergency Department of the Azienda Ospedaliera dei Colli. Afterward, we created a simulation model with Simul8, so that a digital twin reproduces direct and indirect activities in two cases: with and without (What If and As Is model) the aid of the technology.

Results and Conclusions: The model provides a set of Key Performance Indicators (number of performing activities, average alarm resolution time, wait time) on which the compensatory aggregation method is applied to obtain a single final score in both cases. This score is 52.5 in the As Is Model and 80 in the What If model. So, clinical effectiveness has been demonstrated.

Keywords – *Alarm fatigue, safety, communication, clinical effectiveness, simulation model, workflow, vitalsigns.*

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INTRODUCTION

Different people are involved in the patient care process. All of them have to share and discuss information about patient management. These people are not stationary but move around the hospital while engaging in multiple activities at the same time. This can include the manual recording of clinical data and filing medical records which increases the possibility of error and can impact the assistance response times. Furthermore, hearing and correctly identifying an alarm signal and promptly intervening can be more difficult due to the movement of caregivers. As a result, both the interest and the use of information and communication technologies to support health services has increased.

Information and communication technologies offer powerful tools to restructure health service processes. Nowadays, there is a growing range of communication channels, media, and devices, which makes it possible to provide these services. A growing literature on the value of communication in the healthcare sector has already been developed.

Although there has been advanced research in highly specific areas (i.e., telemedicine), the clinical adoption of simpler services, such as voice mail or email, are still not common in many health services. This situation would change if we realized that the biggest information repository in healthcare is the heads of the people who work in it, and the biggest information network is the complex network of conversations that connects the actions of these individuals.¹

Even small clinical teams can generate large and complex communication spaces. The clinical communication space is also characterized by numerous interruptions, poor communication systems, and inadequate practices.

The participants are often separated by time and space. We have synchronous communication in case the attendees exchange messages simultaneously, asynchronous if not (Table 1).

Therefore, care devices and hospital information systems should be integrated to encourage the exchange of information among caregivers and to provide structured data for improving the timely and effective coordination of care.

TABLE 1. Values Measured in a Patient Session

	Sound	Images	Data
synchronous	Telephone	Video conferencing	Electronic cards, documents
asynchronous	Voice mail	Letters, notes, image archive	fax, email

The goal is to provide an easy way to acquire and insert clinical data into the hospital registration system, through the use of mobile, lightweight, portable devices. Linking patients, staff, data, services and medical devices simplifies communications and workflows.

Appropriate approaches to notifications should be evaluated, including the effectiveness of mobile wireless technologies to reduce *alarm fatigue*. The analysis is focused on the current structure and organization of the Emergency Department of Hospital CTO of Napoli (Azienda Ospedaliera dei Colli of Napoli).

This work aims to propose and test a new organizational, technological, and managerial network which is capable of optimizing the hospital's response to the individual's need for health and guarantee caregivers the ability to carry out their clinical activities within the system

The study involves the analysis of the clinical effectiveness (one of the nine domains defined by the EUnetHTA Core Model) of a technology that supports the department activities. For this analysis, a digital twin of the healthcare process was developed using Simul8, to which a set of indicators was calculated. Finally, the compensatory aggregation method was applied to the selected indicators, to obtain a single value that allowed the evaluation of the clinical effectiveness of this technology.

STATE OF ART

In this work, studies and solutions in literature that face these problems have been analyzed. One of the most representative is Hendrich's study.² After equipping each nurse with a Personal Digital Assistant (PDA) for recording activities and a bracelet capable of measuring skin temperature and displacements to assess energy expenditure and distances traveled, this study showed that a

nurse spends 37% of her time in the patient's room and 43% in the nursing station (Figure 1).

Nurse activities: Location

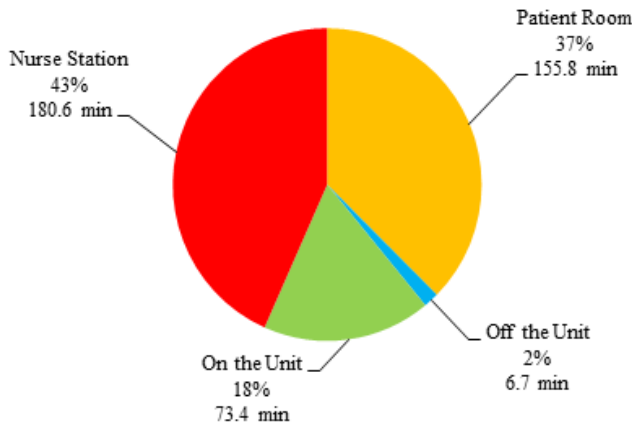


FIGURE 1. Nurse activities: Location.

The main nurse activities are the documentation (i.e., the compilation of medical records, acceptance, and discharge documents) and the coordination of the treatment process (i.e., the communication with other team members to establish the best approach for the patient). A total of 19% of their time (less than 1/5 of the time) was dedicated to direct patient care activities and only 7% was dedicated to the monitoring of vital signs (Figure 2).

Nurse activities: Subcategory

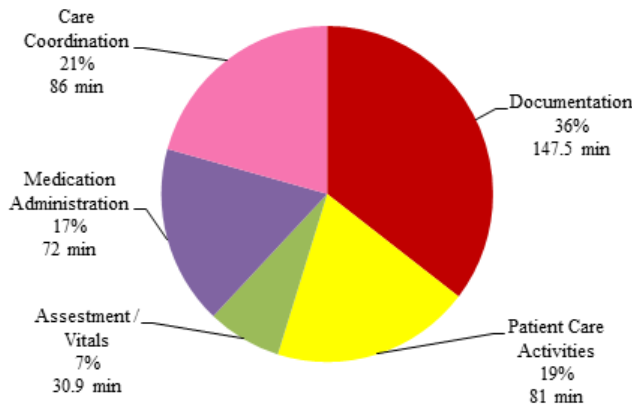


FIGURE 2. Nurse activities: Subcategory.

The Manhattan Medical Research Adoption Study of June 2012 found that the use of mobile devices in healthcare is pervasive (Figure 3). The majority of the interviewed

clinicians (87%) confirmed the adoption of smartphones and tablets in the workplace to improve resources and information at the point of care.³

Smartphone and tablet use in hospital

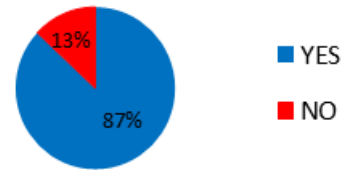


FIGURE 3. Smartphone and tablet use in hospital.

Company policies for the use of mobile devices can be BYOD (Bring Your Own Device) or COPE (Corporate Owned, Personally Enabled). In the first case, the company's initial investment is less, but there are lots of hidden costs and risks, such as distractions, which can lead to clinical risk situations, cybersecurity issues, and data loss problems.

In the hospital, it would be appropriate to provide caregivers with dedicated devices. The main features of these devices should be that they are high quality, light-weight to support mobility; robust and resistant to the action of aggressive detergents or disinfection solvents to reduce infections; impermeable, have a longer battery life, and good network coverage.

Another important problem is alarm fatigue. Sendelbach's research showed that from 72–99% of clinical alarms are false alarms.⁴ The high number of false alarms has led to the *alarm fatigue* problem. Alarm fatigue an overload of work that occurs when caregivers are exposed to an excessive number of alarms it may lead to desensitization and loss of the alarms.

The research should evaluate various approaches to alarm notification, including the effectiveness of wireless technology and to increase the specificity of the alarms without a significant loss of sensitivity. This research aims to figure out these problems by focusing on the analysis of the clinical effectiveness of innovative technology in support of the ward activities.

The technology is modular and includes patient receivers, bed modules, conversation modules (to allow patients to quickly communicate with caregivers and control the

environment), modules with inputs to connect medical devices for monitoring remotely and for the alarm notification, door modules, peripheral modules, corridor lights and displays, personnel consoles, signalers, gateways, and passive bus concentrators (Figure 4).⁵



FIGURE 4. Ascom Telligence technology.

METHODS

Clinical effectiveness is one of the nine domains defined in the EUnetHTA Core Model; a multidisciplinary evaluation model born from the EUnetHTA project funded by the European Union since 2006. The nine domains are developed by a multidisciplinary and multi-professional team.

This work involves the analysis of the fourth domain: the evaluation of the clinical effectiveness of the technology. Effectiveness represents the benefit obtained by using technology in a real work context, whereas the efficacy represents the benefit in ideal conditions.

Simulation can be seen as a valid method for assessing effectiveness, especially in situations where there is a lack of data in the literature and there is no possibility of directly observing the use of technology. Simulating consists of reproducing as accurately as possible the functioning of a system to study its responses to the change of the external environment, even before putting the change into action, through the analysis of suitably chosen performance indicators, called Key Performance Indicators (KPI).

For this analysis, a digital twin of the healthcare process is developed using Simul8. A digital twin is a digital replica of physical systems, devices, processes, people,

places. Simul8 is a simulation software product by SIMUL8 Corporation, used for the simulation of systems that involve the processing of discrete entities in discrete time. Through a model developed with Simul8, it is possible to test real scenarios in a virtual environment. Simul8 allows simulation of the process, defining activities, times, resources, work shifts, to obtain a model representing the entire workflow with reasonable reliability. A Simul8 simulation revolves around the processing of *work items*. They enter the system through the *work entry points*, pass through the *work centers*, can temporarily reside in the *queues* (storage areas), and terminate their path in the process through the *work exit points*. The *work centers* may need specific *resources* to process the represented activity. Simul8 outputs can be graphs, statistics, numeric values.

For this analysis, the analyzed KPIs are:

- number of performing direct activities compared to the total number of required direct activities;
- average alarm resolution time;
- waiting time.

It is possible to apply the compensatory aggregative method on them, to obtain a single decision support score.

$$P = \sum_{i=1}^N w_i V_i = w_1 V_1 + w_2 V_2 + w_3 V_3 + w_4 V_4 + \dots + w_N V_N$$

P = Priority score

w_(i) = i-th weight

V_i = i-th indicator value

CONTEST OF APPLICATION

Mobile handheld devices show greater benefits in high care-intensive environments where time is critical and rapid response is crucial. The application context of the technology is the Emergency Department of Hospital CTO (Napoli). This consists of a First Aid located on the ground floor, equipped with 4 beds in the Observation Area, 2 beds in the red code room and 2 beds in the yellow code room (Figure 5).

The ward is located on the fourth floor and has 18 beds divided into 7 rooms (4 with 3 beds and 3 with 2 beds). There is also a nurse station (Figure 6).

(morning, afternoon, and night) which reflect the different work shifts and staff availability.

All staff members filled out a questionnaire. Their answers and the direct observation of the process allow the definition of the frequency and duration of their activities.

The direct activities identified were:

- therapy administration;
- vital parameters control;
- patient hygiene;
- withdrawal, catheterization, medications;
- tours;
- alarm management;
- bed calls; and
- health status updates.

The indirect activities identified were:

- emergency in the First Aid department;
- medical record filling;
- drug preparation and therapy;
- medication warehouse management;
- instrument management;
- briefing with colleagues;
- patient disposal activities;
- patient acceptance activity;
- conducting diagnostic tests;
- transfers to other facilities; and
- exam requests.

For direct activities, the *work item* corresponded to every care need at the bed. Every *work item* was processed in a work center and for each of them an operating time may be defined, depending on three different levels of patient complexity. Every activity was made by one or more people (nurses, doctors, and auxiliary staff) recruited on predefined shifts. These activities involve the movements of caregivers into the department and the operation time reflects the distance between the nurse station and the room from which the assistance need originated. Regarding indirect activities, the work items no longer represent patient needs but the repetitions of the

individual activities and their duration was independent of the patient complexity level.

After having entered all the required data, the simulation model could run on different time frames and at different speeds through a dedicated cursor. It was also possible to obtain indications regarding the trend of the variables that characterize the functioning of the model through a series of graphs selected by the user. During execution, the icons and animations facilitate understanding of the workflow.

Before using the model, it was necessary to verify whether the model could represent a reasonable approximation of reality. An approach divided into two successive steps was adopted for its validation outlined below.

- Formal validation: evaluation of the code correctness.
- Structural validation: comparison between the behavior of the simulation model and the real system, to assess whether and how much the model can be considered a good approximation of reality. The structural validation consists of two successive moments:
 - open-box validation: the staff evaluate the model;
 - black-box validation: the results are compared with the data obtained from the real system.⁶

According to these validations, it was possible to find that the simulation model implemented constituted a good approximation reality.

THE AS IS MODEL

The As Is model consists of the evaluation of the workflow characteristics and performance in the current configuration. The As Is model created is described in Figure 7.

To define the model, 5 steps needed to be implemented.

1. Identification of direct and indirect activities.
2. Identification of the frequency and duration of all activities through direct observation and questionnaire.
3. Identification of the resources that complete the activities, taking into account the work shifts.
4. Validation of the model.
5. Analysis of KPIs.

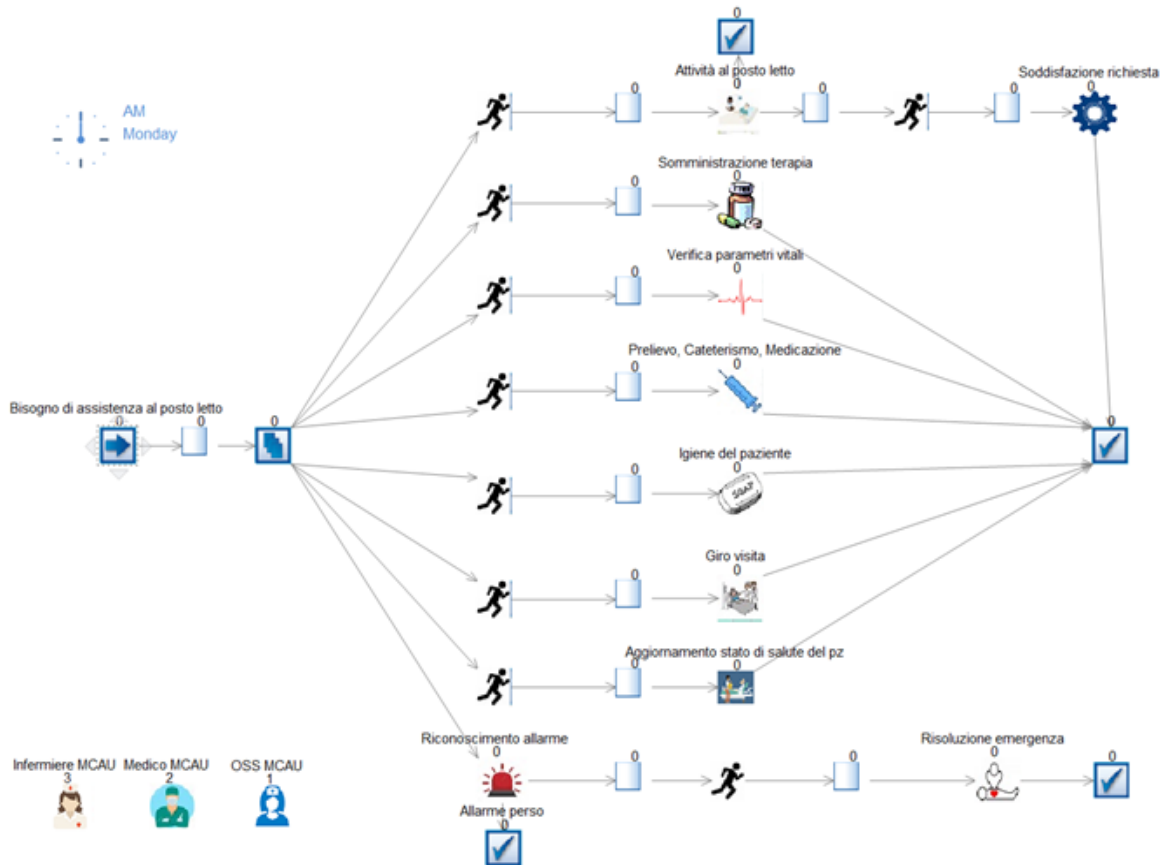
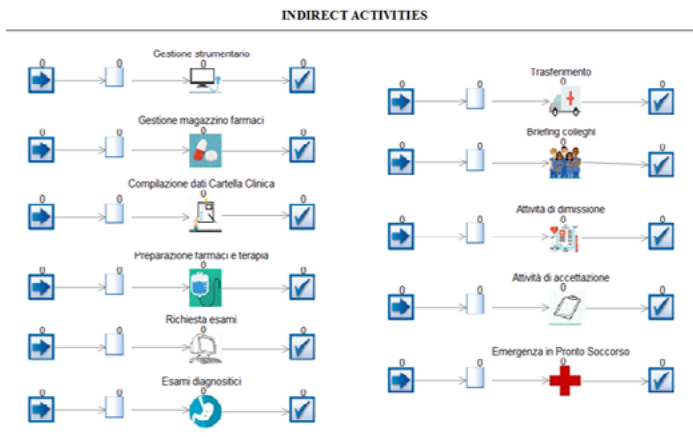


FIGURE 7. As Is model.



Each *work item* generated by the Start Point related to direct activities represented a care needs at the patient's bedside. Considering that there were 18 beds in the ward, it was estimated that these needs occurred every 5 minutes. A label was associated with each *work item* and set on a distribution that represents the frequency of each patient's bedside care needs (Figure 8).

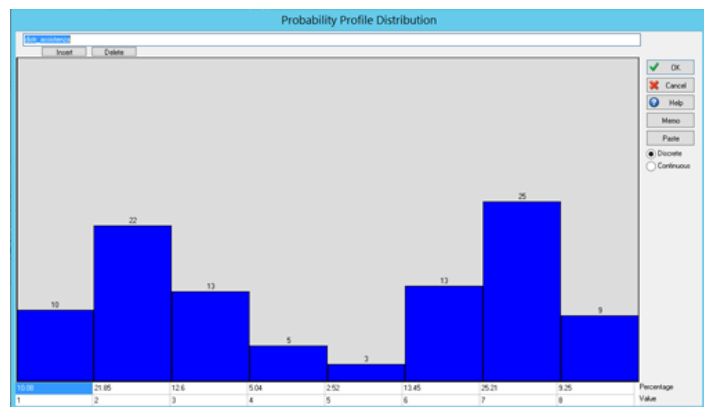


FIGURE 8. Distribution of patient bedside care needs.

Each care need may come from a different bed, so each generated *work item* was associated with an additional label, set on a different distribution which defined the distance from the nurse station and takes into account that rooms 1, 2, 3 and 4 have 3 beds and rooms 5, 6 and 7 have 2 beds (Figure 9).

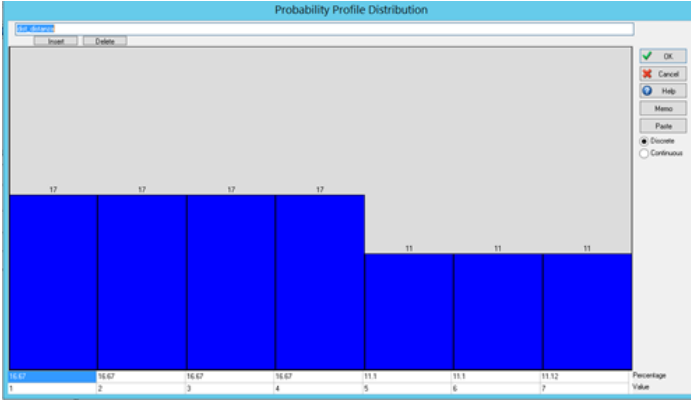


FIGURE 9. Distribution of nurse station-bed distances.

The movements were modeled through an activity whose operation time was defined by the time taken to reach the room the call comes from.

The 7 possible paths defining the movements from the nurse station to the patient’s room have the following lengths (measured by AutoCAD): 15.64 m; 23.82 m; 30.62 m; 35.53 m; 41.76 m; 44.47 m; 42.37 m. Considering that the operator average speed is 5 km/h, the travel times are calculated. Operation Time is defined for the movement activities and depends on the distances (Figure 10).



FIGURE 10. Routes on the Emergency department map.

Operation Times of the other activities, on the other hand, take into account the level of complexity of the patient (Figure 11).

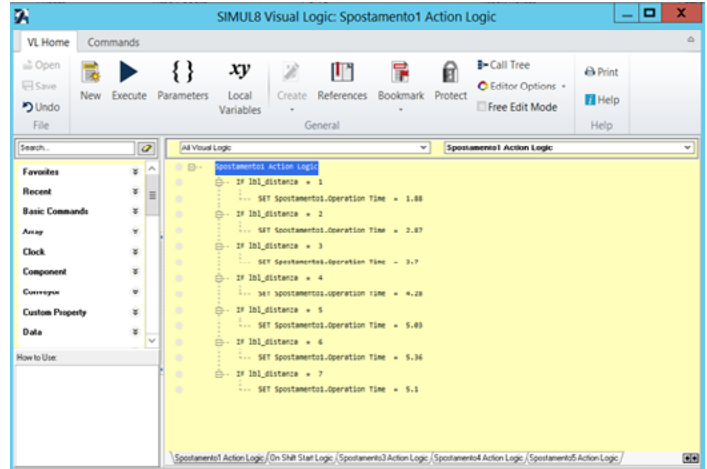


FIGURE 11. Visual Logic code for defining the movement activities Operation Times.

The model determined that only 50% of cases did the bedside activities end directly at the bedside: the caregiver was often forced to make multiple movements to satisfy the patient’s needs. The model took into account the alarm acknowledgment times (due to the lack of a centralized monitoring system) and the possibility of losing the alarms (due to the alarm fatigue problem). Moreover, each activity was associated with one or more resources (Figure 12).

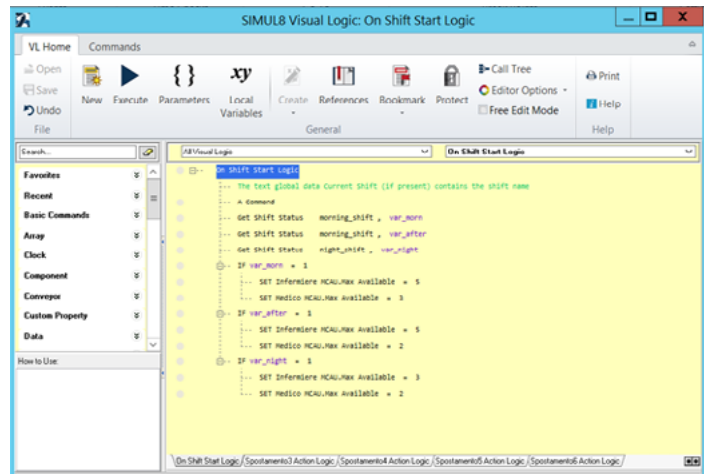


FIGURE 12. Visual Logic code for defining shifts.

Three shifts were identified.

1. Shift from 07.00 to 15.00, in which 5 nurses and 3 doctors are available.

2. Shift from 15.00 to 23.00, in which 5 nurses and 2 doctors are available.
3. Shift from 23.00 to 07.00, in which 3 nurses and 2 doctors are available.

One social and health professional was always available.

Regarding indirect activities, the *work item* no longer represented a patient’s bedside needs but the single repetitions of the individual activities. Resources, frequency, and duration were also appropriately associated with the indirect activities and were independent of the patient complexity level.

The simulation time was 24 hours, every day for one month. According to the validation, the simulation model implemented constituted a reasonable approximation of the real system. It might, therefore, be suitably modified to study the response to the introduction of technology. Improvements to the workflow were introduced in the What If model to check the introduction of the technology’s impact on KPIs.

THE WHAT IF MODEL

The What If model created is shown in Figure 13.

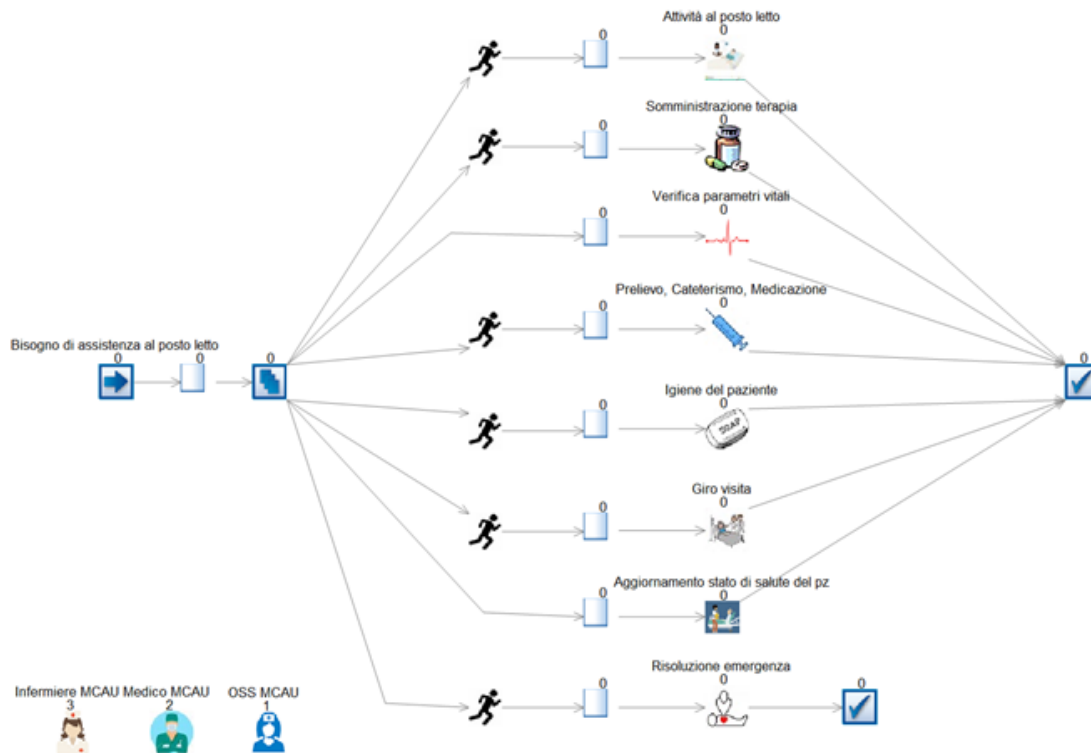
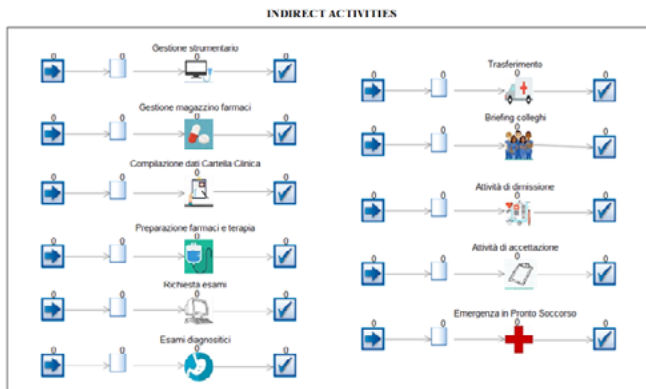


FIGURE 13. What If model.



This model was created by properly modifying the As Is model, taking into account the activities on which the technology operates.

The main differences with the As Is model are:

1. The calls end directly to the bed, without making further movements. It may happen because the caregivers already know the patient’s need even before going there.
2. The vital signs can be remotely checked.
3. The patient’s health status can be updated via devices.

- There is no longer an alarm acknowledgment time since the technology reports the bed from which the alarm goes off. Furthermore, there are no more lost alarms.

Indirect activities remain unchanged.

RESULTS

The KPIs are:

- The number of completed direct activities compared to the required activities. The ratio between the two numbers ranges from 0 to 1: it is 1 when the number of completed activities is equal to the required ones (ideal case), 0 if none of the required activities is completed (worst case).

$$V_1 = \frac{\text{number of completed activities}}{\text{number of required activities}}$$

- Average time to resolve an alarm.

$$V_2 = 1 - \frac{\text{Average alarm resolution time}}{\text{Maximum alarm resolution time}}$$

- Waiting time for direct activities.

$$V_3 = 1 - \frac{\text{Average waiting time}}{\text{Maximum waiting time}}$$

The weights for the application of the compensatory aggregation method, chosen in collaboration with the staff, are: 50 for V1, 20 for V2, 30 for V3. The sum of the weights is 100 and the ideal values of V1, V2 and V3 is 1.

At the end of the simulation, the data related to the identified KPIs are presented.

The As Is model showed the results below

- A total of 70% of bedside care needs are fulfilled.
- The average resolution time for an alarm was 28.57 minutes.
- The waiting time to complete direct activities was 9.23 minutes.

KPIs for the As Is model are outlined in Figure 14 and the Compensatory Aggregation Method of the As Is Model is presented in Table 4.

TABLE 4. Bed Locations

V _i	0.7	0.065	0.54
w _i	50	20	30
$0,7*50 + 0,065*20+0,54*30 = 52.5$			

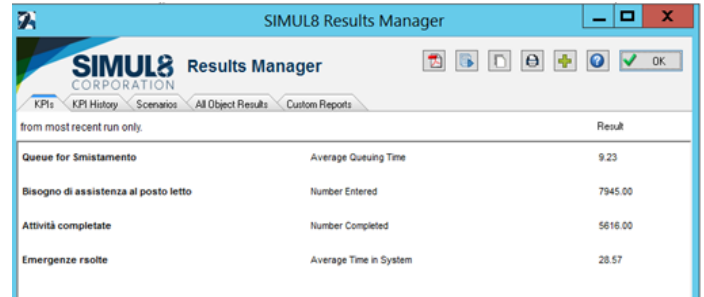


FIGURE 14. Compensatory Aggregation Method – As Is Model

The What If model shows the following results:

- A total of 90% of bedside care needs are fulfilled.
- The average resolution time for an alarm is 15.86 minutes.
- The waiting time to complete direct activities is 5.16 minutes.

KPIs for the What If model are outlined in Figure 15 and the Compensatory Aggregation Method of the As Is Model is presented in Table 5.

TABLE 5. Compensatory Aggregation Method – What If Model

V _i	0.9	0.64	0.74
w _i	50	20	30
$0,9*50 + 0,64*20+0,74*30 = 80$			



FIGURE 15. KPIs – What If model.

Considering that in the ideal case the final score is 100, from the compensatory aggregation method it results that this is 52.5 in the current model, 80 in the model that simulates the introduction of technology. The clinical effectiveness of the innovative technology for the communication and distribution of alarms and vital signs is therefore demonstrated.

DISCUSSION

The analysis of the clinical effectiveness of the technology studied in this work was based on the compensatory aggregation method applied on the KPIs obtained by the simulation models created with Simul8 (see Table 4 and Table 5).

The above-mentioned approach allows for:

- estimation of the organizational changes, which are generally complex to analyses in other ways;
- assessment of the operating conditions of the department;
- determination if, and how much, the resources operate in compliant conditions;
- determination of which resources intervene to improve the workflow; and
- determination of which activities should be modified.

This methodology was also very educative for the caregivers who had the opportunity to systematically analyzes their work organization both during the analysis phase and the discussion of the simulation results.

Having more precise measurement results of the real system behavior would be desirable: unfortunately, it is very complicated to obtain in an operating environment such as a hospital ward, even more in a high-intensity care environment like an emergency department. To obtain precise estimates, it would be necessary to measure the completed activities at the bedside in daily life with precise tools and for a longer time.

The main limitation of this work, like most of the works based on simulation models, is the difficulty to compare the results of the simulations with the results of the real world, despite the effort of the formal and structural validations. The analysis began from a real-world measurement of the process: it was empirical and based on subjective

assessments of the caregivers and on the observation of ward activities. The reliability of the model and results depended on the reliability of the indications given by the caregivers and also the observations made internally in the ward. However, the model and methodology used can be considered a sufficient basis for further customizations in many case studies.

CONCLUSIONS

The clinical effectiveness of the technology supporting the ward activities was demonstrated with the simulation method, in situations in which validated scientific literature was not yet developed.

The As Is model has a good adherence to reality – both formal and structural validation were used. According to the caregivers, the As Is model represented a good approximation of reality, but the comparison should be made on indicators that can be accurately measured. It is not always possible, especially in emergency medicine departments. The What If model could be improved with the analysis of some data from realities where the technology is already in use.

The simulation model offers the possibility to find out the resources and activities that need to be modified for improving the workflow. The simulation model has increased the awareness of hospital employees regarding the complexity of the processes.

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