Challenges of Clinical Decision Support System Development

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Abstract

One of the high-growing areas in medicine is research and development of advanced IT technologies for clinical decision support. Clinical decision support system (CDSS) must be able to store the necessary clinical data and also to analyze this data, and process and interpret the results for a specialist. This article is focused on interdisciplinary research and development challenges in developing a complex information system for searching and selecting a suitable donor for bone marrow transplantation using an advanced DNA-based donor search model. The particular challenges are summarized and the approaches to tackle them are described.
Keywords: CDSS development, decision support, biocybernetics methods, DNA search, bone marrow transplant.

1. Introduction

Clinical decision support systems (CDSS) are computer systems designed for clinician decision making about individual patients [1]. More precisely, these systems can be described as adapted decision support systems (DSS) defined as extensible systems with intrinsic capability to support ad hoc data analysis and reduction, as well as decision modeling activities [5] specifically designed for physicians to make or improve clinical decisions. CDSS are highly specialized for the various processes of healthcare. The development is always very complex and full of challenges of a different kind due to the necessary interdisciplinary holistic approach characterized by considerable demands on knowledge both in medicine and in the field of IT. Therefore, we present the challenges of CDSS development in one particular case, namely in research and development of advanced IT technologies for support of the bone marrow donor search. Complexity of this system is given not only due the medical-technician

interdisciplinarity, but also in terms of DSS classification (according to [9]). It is basically a knowledge-driven DSS (could simulate human thinking in a particular domain) but it has elements of model-driven (help to analyze and choose between different options) and communication-driven DSS (focuses on different users collaboration and makes the decision-making faster and more productive), i.e., can be defined as a hybrid DSS. Some challenges have also arisen due to the integration of biocybernetics methods and approaches into the standard information system (IS) methodologies and technologies.

2. Clinical background

Due to the CDSS development description and its specific challenges, it is appropriate to provide at least a basic background of the bone marrow donor search. The presented CDSS is primarily based on biomedical knowledge of the issues of human leukocyte antigen (HLA) system, of the hematopoietic blood stem cells transplantation process, knowledge in the cybernetics area (mostly analytical), and in information technology. Thus, in our case it means a cooperation of physicians and technicians in the HLA laboratory performing HLA typing of donors and patients, physicians performing a search of potential donors for stem cell transplantation, other health care professional staff, and also part of the research team involved in analysis and development methods, as well as a group of IT professionals engaged in applications implementation, communication interfaces, connection of existing information, communication system parts and complete system support.

The key process before transplantation of bone marrow or peripheral blood stem cells is to find the optimal donor for particular patient from a database of potential donors, i.e., to perform a "search". An absolutely essential requirement for successful transplantation is a degree of HLA match between the donor and the patient [7]. The fundamental functionality of the CDSS for the bone marrow donor registry is to provide a list of potentially suitable donors with a search algorithm in the shortest possible time and to facilitate the very choice of a suitable donor as fast as possible [10].

The issue of match in the HLA system between the patient and the bone marrow donor at the highest possible level has become more complicated with the advent of the DNA techniques used for HLA typing. Given the proven importance of their use (compared to the previously used serological techniques) [4] a need arises to create a new CDSS including models matching the current global trend of using the DNA information and the needs of patients for all worldwide marrow donors registries.

When selecting a donor many HLA and many non-HLA factors (e.g., gender, age, cytomegalovirus status) are considered. Each person gives a complete genetic program observable as phenotype, consisting of 2 haplotypes of HLA genes (one from the father and one from the mother), together known as the haplotype pair. The compatibility of the patient-donor is observed on 5 loci (genes) for each haplotype – HLA-A, B, C, DRB1, and DQB1 locus. However, for most donors this knowledge is incomplete. Hence, it is necessary to estimate concrete alleles – specific gene variants for the unknown ones. The knowledge of specific alleles is conditioned by the level of typing resolution. So, if e.g., the HLA-B locus is typed as 27s (serological typing) or 27:HMHK (National Marrow Donor Program (NMDP) code) is also necessary for donor search to determine the likelihood of specific allele occurrence (e.g., 27:02) in the particular case. Simply, if the HLA information is incomplete, it is necessary to estimate the unknown alleles (both patient and donor), and determine the probability of the patient-donor match (for the entire donors dataset). The desired match level may not be the only level of 10/10 (all 10 donor's alleles are identical to the 10 patient alleles), but also other, e.g., 9/10B meaning one mismatch on B locus (9 alleles of the donor and the patient are identical).

The presented system was developed in cooperation with the Czech National Marrow Donors Registry (CNMDR), which is currently the largest marrow donor registry in Central and Eastern Europe, enabling around 100 unrelated hematopoietic blood stem cells transplants every year. The CNMDR operates throughout the Czech Republic through ten contractual donor centres at regional and immunological transfusion hematology wards. Work of individual donor centres

is centrally coordinated by the CNMDR coordination centre, which also provides communication with the transplant centres and international registries. The HLA typing is carried out in an accredited HLA laboratory [8].

3. Challenges of CDSS development

Because an essential factor in the entire donor search process is time, one of the major challenges was communication process optimization. The other challenges, which we had to face during design and system solutions, were necessary restrictions of each users' certain specific requirements because of the compliance requested by the World Marrow Donor Association (WMDA) international accreditation standards and standard operating procedures of donors' registry. Other limitations were caused by personal data exchange in an automated national and international communication, by specifics of processing of necessary medical data and the knowledge or even the actual negotiation with the physicians or laboratory technicians. Others challenges were related to the actual CDSS design, e.g., using biocybernetics methods for integration of new donor searching system components or to standard problems solved during a DSS development, e.g., the issue of the necessary database or the verification of decisions correctness and accuracy.

It is more complicated when it is not possible to start the development completely anew but instead must be accept that there are in the past defined - and partially invalid - data sources (in the case of the CNMDR collected from 1992); it is necessary to get familiar with how everything procedurally works. It is also required to ensure the least possible interference with the current operation and clinical practice, and simultaneously optimize the processes. In our case a great emphasis on these issues is put by the CNMDR legal entity in the form of a public service company. So, besides the required integration of new donors search methods and related both medical and technical challenges, also challenges appeared based on the largest possible procedures and applications preservation while complying with the CNMDR standard operating procedures and meeting the requirements of international accreditation organization (WMDA).

In summary, the specifics of the developed system compared to other CDS systems are 1) a method for requirement specification – requirements for IS specific components and functions are missing. Specifically requirements regarding preservation of part functionality from the existing system used in clinical practice, 2) IS functionality is limited not only by national standards but also by WMDA standards. Specifically, IS has to have an interface for automated international communication, 3) the CDSS is highly distributed, and 4) IS knowledge/model/communication-based hybridity, as mentioned above, is not common in CDSS.

The whole CDSS for bone marrow donor search development and challenges associated with it are demonstrated in Fig. 1. The diagram shows links for development of subsequent activities and obvious CDSS development complexity. It can be seen that the CDSS knowledge base was created according to analysis results and gained medical knowledge obtained from requirement specification, the model was based on the proposed methodology and knowledge about haplotype and phenotype diversity with regards to DNA typing resolution level (NMDP codes). The inference engine operation needs data from the knowledge base and from the model. The challenges connected with single steps of the unified CDSS development are described below.

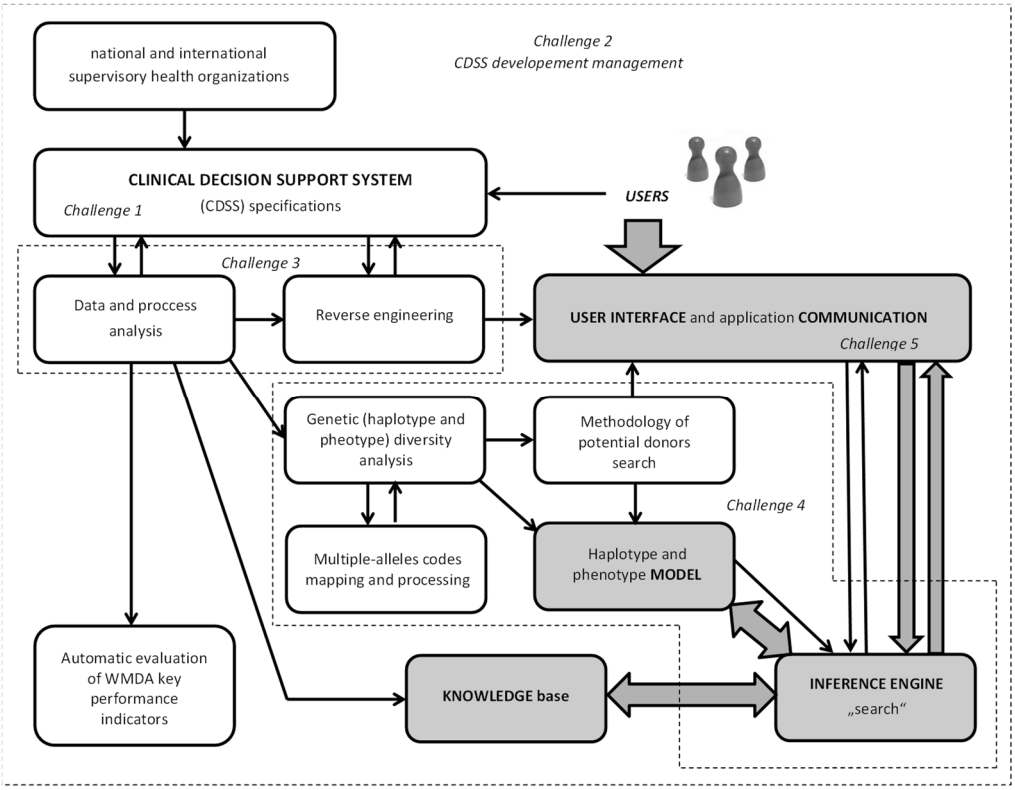

Fig. 1. Complexity of CDSS for bone marrow donor search development

During designing a CDSS there are always the same issues as during a classical DSS development but with some health care specifities as well the challenges attributed to the actual clinical focus. Hereby, one group of challenges appears commonly in the DSS design and can be always considered as critical, particularly for the knowledge-driven DSS development. In this case it must be clear what data and knowledge are actually available and what will be available in the future for decision support. In general, it is necessary to have all available information incorporated into the information and communication systems so that they can serve as parts of the system knowledge base.

3.1 Challenge 1: Requirements specification

The very first challenge was the requirement for establishing the CDSS itself. A significant difference from the standard IS development was the method of requirements specification. As stated earlier, there are no requirements for IS specific components and functions. Specifically, regarding the resulting activity, global needs and needs for preservation of part functionality from the existing system used in clinical practice. Therefore, requirement definition was carried out continuously during IS development, repeatedly in several steps, including frequent validation of gradually developed components and integration of permanent changes.
In doing so, rough understanding of IT development techniques was required on the side of medical professionals. All during the system analysis and the technical development phases, technical, and practical requirements were jointly formulated by medical professionals, and medical-IT coordinator. For instance, event-driven process chains (EPC), and entity-relationship modeling (ERM) techniques were selected for their intuitiveness as well as for their flexibility, and past implementations by the research team. Details are described in Section 3.3.
The general requirement was based on current global needs, e.g., on the possibility of using donor/patient DNA information. It meant to create a single CNMDR system capable to recommend the most suitable HLA typed donor to the transplant centres (primarily for Czech patients) using the known DNA information with a focus on optimizing the time component of the search process. Because time – hence the speed of identifying a compatible donor and urgent

performing of unrelated transplantation – is one of the key factors for optimal transplantation results.

It is necessary to mention that dealing with the general requirements was heavily influenced by communication obstacles. The process of final donor selection includes a cooperation of several registry components such as donor centres (DCs), national transplant centres (TCs), and the coordination centre (CC), which also coordinates the registry activities on international level. Each of these components had their own information structures (from paper records via Excel spreadsheets to different variants of databases), its own processes and operating methods and each produces its own data in its own record form.

A more detailed requirement specification was based on an initial analysis of efficiency factors limited by the CNMDR ICT. The following major limitations were identified: 1) inadequate "search" algorithm based solely on serology technique of HLA typing, unsuitable and insufficient assessment and screening of donor suitability still based largely on subjective physician decisions, 2) absence of any analysis of the registry database (genetic diversity, frequency of haplotype, alleles etc.) and as a consequence the absence of prognostic information provided to TCs in terms of probability and speed of finding a compatible donor, 3) lack of registry processes, donor recruitment and existing typing strategy efficiency analysis, absence of an interim analysis and comprehensive statistical analysis of the individual steps of the search process – required by accreditation organizations (WMDA key performance indicators) and currently performed manually and 4) data records fragmentation, i.e., absence of a DCs database, its linkage with the CNMDR database (CC and HLA lab database), information and knowledge connection of the individual search process components, absence of IT communication among CC, TCs, selected European databases, and worldwide registers and related IS security.

The initial analysis was followed by a deeper analysis carried out in cooperation with particular CNMDR components. It can be said that the CNMDR had the whole area of information technology grossly inadequate. So, in this particular case it was necessary to focus on three main areas: 1) the facilitation of communication between the CNMDR components, 2) the facilitation of donor selection for physicians and 3) maintaining the highest security and necessary anonymity throughout the search process, implying already mentioned hybridity of the IS.

Herein, it is important to note that the possibility of specific requirement implementation had to be analyzed and compared with the prescriptive requirements and restrictions of supervisory health organizations. This always has a priority and it is one of the fundamental limitations of the CDSS development.

3.2 Challenge 2: CDSS development management

One of the most crucial challenges for every DSS development is identifying the specific requirements that the system must satisfy. For the CDSS this is even more important mainly due to medical-IT interdisciplinarity. In some cases, physicians are not aware that the medical context is not common knowledge. Similarly, engineers are unable to clearly understand the importance of some system parts necessary from physicians' operational point of view. The solution is, therefore, having a suitable coordinator familiar with both fields, either a technician with a deeper knowledge of particular biological issue or a physician with a deeper knowledge of information systems. Identifying the specific requirements is the first task in the system analysis. The coordinator is actually a standard system analyst. Use of the title 'standard system analyst' is given by the job description as well as by the fact that generally main activity of the analyst should be mutual understanding of all considered in development.

The uniqueness of the CDSS development is that it is not possible for a standard system analyst to learn in-depth all the necessary medical domain knowledge in a reasonable time. So, it is necessary to have medical professionals as a part of the analytical team throughout the analysis and development of the CDSS and to communicate with them. To summarize, the only possible path for the CDSS development is the use of agile methodologies (we used Feature Driven Development).

In our case a biocybernetics expert was chosen as the system analysts. He had the required knowledge, in-depth knowledge of biology principles and considerable knowledge of IT. This expert with the medical domain knowledge was indispensable. When an IT expert, unacquainted with the medical background, receives a requirement (e.g., "the result must be HLA match"), he does not know what questions to ask and what specifically must be addressed to determine the exact requirement specification. Moreover, the added value of this choice was his knowledge of the system approach and applying the interdisciplinary principles in solving the IS design challenges. It was also preferable to have this person in the CDSS development management.

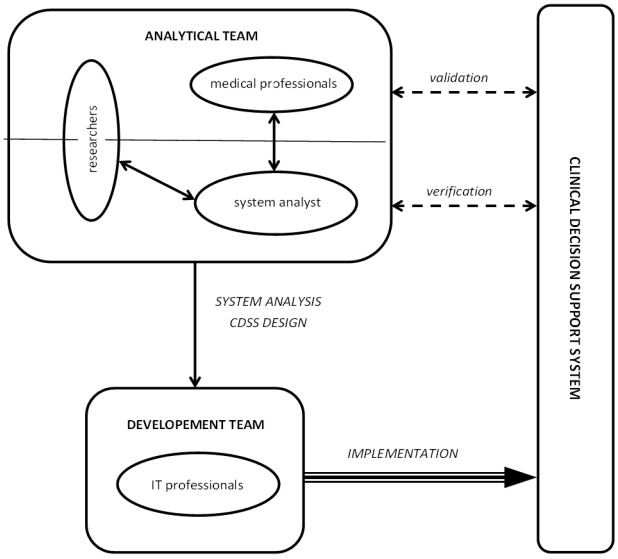

Fig. 2. CDSS development life cycle

The CDSS development life cycle is presented in Fig. 2. The analytical team consisted of medical professionals (future users – physicians and other health care professionals, e.g., other DCs, TCs, laboratory staff), the research team involved in the analysis, and a system analyst, who processed the system analysis and design of the CDSS. During performing this analysis he closely cooperated with medical professionals. A key decision was having a system analyst during the CDSS development for the medical-technical communication coordination. The development team implemented the designed system components, whose functionalities were verified by the system analyst and then validated by future users. Implementation of a system analyst increased the effectiveness of the development. IT professional could remain unaffected by the necessary medical knowledge issues.

3.3 Challenge 3: System analysis, conceptual design of CDSS

In order to handle the requirements of the users, to include prescriptive requirements of the supervisory organizations in the development of the IS and to change the processes and clinical operations of the CNMDR to a minimum degree, it was necessary to perform the system analysis as the first step. It meant to make an analysis of the existing system, which structure and functions were not obvious to users nor to the developers. The analysis was based on the sequential use of analytical techniques for data and process analysis, reverse engineering and database modeling and design tools.

The goal of the process analysis was to monitor the activities and data interface (the data analysis is considered as a part of the process analysis) and it was generally a starting point for further optimization and reengineering. The mapping of the existing processes was carried out in cooperation with medical professionals and the system analyst on the basis of the CNMDR standard operational procedures. To perform this analysis, the interdisciplinary cooperation was

crucial. Based on the analysis results, consequently specific requirements were more precisely specified and modified.
The current CNMDR processes were recorded with the EPC methodology, the various activities listed in these diagrams were discussed in detail. The diagrams contained all activities of the whole process, i.e., the current activities supported by the ICT but also those unsupported, in the great majority solved manually. Within the CDSS, the conceptual design diagrams were then complemented by proposals of application support for these processes. In the third step, the processes were processed from the viewpoint of unified IS support and the required functionality including links to the designed data model were specified.
According to the data and process analysis (especially inconsistencies of data sources and data duplicity in various sources) it was necessary to deal with the unification of the data base. For this reason, the "reverse engineering" of the existing system was performed. More specifically, a complete mapping of the current IS status quo was performed, which was focused on data sources in/outside IS, analysis of existing system modules, database structures and analysis of existing communication components. The analysis was performed using the computer-aided software engineering (CASE) tools. For existing applications particular system functions, the data flows between them and the data flows between functions and external interfaces (system inputs/output) have been documented. The functions were shown as diagrams in a hierarchical structure and described by short comments. Then, the diagrams of the ERM describing the structure of the database entities were processed.
As a part of the CDSS conceptual design the data model of the IS was designed. A new unified database was proposed based on performed analysis and capturing new requirements and new functionality of the system (e.g., the components required for donor search according available DNA information). The IS database model was designed for the PostgreSQL database management system (originally database components used Firebird) and processed in the CASE tool Toad Data Modeler. The tool defines the database structure using the ER diagrams and all database functions required for the IS operation and allows generation of SQL/DDL scripts to create a functional PostgreSQL database. Considering the CNMDR as a public service organization, this solution was chosen due to the importance of using an open-source tool. Also smooth system extension was taken into account.
According to the performed analysis results, the proposed data modification, and gained domain knowledge, the CDSS knowledge base was created.

3.4 Challenge 4: Design of clinical decision support model and inference engine

For the model-driven part of CDSS it was necessary to design a clinical decision support model and an inference engine ("search") and for the CDSS operation to invent an entirely new approach, both in terms of methodology and perspective of integration into the system. As the core of the system should use an advanced DNA-based donor search model, a lot of challenges were encountered during its development. Most of them were caused by working with medical data in the field of immunology, HLA issue specifically, and by having their own medical complexity depth (a very brief medical background of search process can be found in Section 2). Description of each specific issue of challenge 4 is supplied with a brief description of the problem and its solution without going into unnecessary details. These issues are all given by specific clinical focus and by biocybernetics method used during research of the new search method. However, similar issues are addressed by the model-driven CDSS.

Methodology

Finding suitable stem cell donors comprises three independent processes: the donor pool HLA typing, the donor HLA haplotype inference, and the search for donor HLA phenotype matches. For practical and technical reasons, these processes are often decoupled leading to information losses along the way. So, this challenge was associated with a proposal of a method and methodology that would eliminate these losses.
The designed common haplotype Expected-Maximization (chEM) method eliminates some of the technical challenges by considering all three steps together. From the perspective of the

model and the inference engine utilization, it meant to propose the procedure for identification of probabilistic models of unrelated donors' haplotypes with ambiguous typing, to propose a procedure for the required haplotype pairs identification and to obtain probabilistic models of patient-donor HLA phenotype matches at the required match level used in the search. This method is scalable in the number of HLA loci, the number of alleles (concrete specific gene variants), and typing ambiguity, overcoming the known curse of dimensionality for the problem of the HLA haplotype inference. A detailed description of the methodology can be found in [2].

HLA data and HLA typing level

The complexity of data processing, identifying the haplotypes and the phenotypes required for the decision support is based on the use of the DNA techniques of HLA typing. The DNA locus may be identified specifically at the high typing level (specific allele) or at lower resolutions, e.g., in the form of multiple-allele codes (NMDP codes), which define the possible allele variants. Therefore, it was necessary to deal with this situation. Preprocessing such data was implemented directly in a PostgreSQL algorithm that decomposed the code into all possible variants of the specific alleles for the purpose of probabilistic models. These are then further used for patient-donor compatibility modeling. With the constantly increasing volume of specific alleles are the NMDP codes regularly updated on NMDP bioinformatics website [6] and it was necessary to handle a mechanism that allows the system to regularly update the list of those codes.

However, the DNA typing techniques are relatively new, and the question arose of how to deal with historical HLA data that is obtained by outdated and inaccurate (especially for HLA-C genes) serological technique. For serological data it was necessary to find a conversion mechanism allowing uniform treatment of all data as DNA data. Correctness of serological data conversion was given by the use of serology-DNA conversion tables processed by an international team of medical experts, listed on the website [3]. Within the initial probabilistic models identification the conversion of the serological data of donors was performed. All new donors are typed by DNA techniques.

Identification and verification of probabilistic models

Some challenges were related to the identification of haplotype and phenotype probabilistic models and 5 loci haplotype pairs estimation. These were mainly related to the inability to identify haplotypes/haplotype pairs according to knowledge of existing haplotypes. That is why the identification process was partitioned into several steps. The first step concerned identification of the model over a defined set of donors. Then, in the cases of unidentified haplotype pairs special methods for rare haplotype identification were used, which perform the identification on the basis of B-C and HLA-DRB1-DQB1 genes linkage frequencies. The probabilistic model is then extended for a new rare haplotype or haplotype pair. The most common causes of impossibility of identifying donors' haplotype/haplotype pairs while developing probabilistic models were serologically entered values of HLA-C locus (according to consultation with field experts 30% error rate) on one site, for donors with a high typing DNA level the occurrence of new or rare alleles on the other site.

A function library for using haplotypes probabilistic model that allows key calculations needed to search was developed. The implemented functions are used primarily to calculate the frequency of alleles or haplotypes in the population, which is necessary for the analysis of genetic diversity, for the estimation of missing data (alleles), and for estimating the patient-donor HLA compatibility, which is required for the actual search. For practical use it was necessary to periodically update this data (prior information autocompletion). For this reason a mechanism was integrated that triggers the model update daily at 2.00 a.m. The frequency of models updating must always be solved in accordance with time-consumption and clinical practice.

An important challenge is models verification. In the case of the CDSS it is usually performed by a confrontation with expert knowledge of HLA experts and comparison with the results of the available knowledge of literature. These subjective methods were used, e.g., comparison of

the outcomes of the previously performed searches according to physicians with the models predictions. An objective verification of probabilistic models was made by a verification typing of donors, i.e., HLA laboratory testing for determining the DNA alleles of all loci. The results of probabilistic models for the patient-donor match with the data from the knowledge base are necessary for the proper operation of the inference engine. Comparing the inference engine results with physicians' results was an essential activity for the CDSS functionality verification.

3.5 Challenge 5: System communication and data exchange security

At this point it is convenient for better understanding to describe the donor selection communication path in a simplified form: the DC recruits a donor who is typed by the HLA laboratory and then recorded in the CNMDR; the TC or international registry requests for a donor search, the CC working with CNMDR database issues this search and the TC or international registry decides based on the search recommendation on selection of few potential donors for verification. The verification is carried out in cooperation with the DC and the HLA lab. After obtaining the results of verification, the TC chooses one particular donor.

On the national level, the communication within the donor selection process was resolved by individual access of transplant process participants to a common database. The operating HW CNMDR server containing the PostgreSQL database is located and integrated into the University of West Bohemia standard ICT infrastructure equipped with the necessary technological background, such as backup power supplies, connection to backup systems, monitoring of operational status, permanent surveillance service etc.

Because of the requirement of simple usability and readability of the CDSS results for users and the fastest possible information transfer between all new parts of the system as web applications (specifically for DCs, TCs and partially HLA lab) have been designed. The TC searching the donor has immediate access not only to the result of the search conducted by the CC, but also to the current status of donor verification carried out in cooperation with the DC and the HLA lab. The security policy and access to individual applications are based on the sensitivity of the data used and presented. On the operational HW server the access to the secure applications is limited (specific IP addresses + user name and password with a definition of the role of the user) and simultaneously the data transmission is encrypted via VPN (accessible via the relevant certificate on HW key protected by a PIN).

On the international level, with worldwide registries the communication was automated connecting to European Marrow Donor Information System (EMDIS), the automatic email communication system. The above mentioned HW server containing the PostgreSQL database also contains the EMDIS server portion and the EMDIS mail server. The mail server itself allows individual restrictive setting of mail delivery only to selected and authorized clients (foreign registries), which increases security of communication system. The communication security is defined by the EMDIS standard and is processed by asymmetrical encryption of the messages in flexible message language format (FML messages) using PGP/OpenPGP.

Due to the newly created system functions there was also a need to develop access to anonymised data that is used, e.g., for general data analysis or for publicly accessible visualization of WMDA key performance indicators. It is implemented as a database interface that accesses the auxiliary database, which is generated as an anonymised copy of the operational data. Due to the anonymised outputs the data cannot be directly linked to the donors or patients and thus they are freely available for general hypothesis testing or statistical calculations.

4. Conclusion

The objective of the paper was primarily to present various challenges of CDSS development, shown namely on CDSS for searching and selecting a suitable donor for bone marrow transplantation, as the methodological guidelines for researchers in the field where hybrid DSS is needed, IS development is driven by permanently changing user requirements, and additionally the design should be (partially) based on any technical components already used

in clinical practice. The described CDSS was deployed in 2014 and it is used in clinical practice. In 2015, the search algorithm and IT system solution and its correctness were certificated as a part of CNMDR accreditation by international accreditation organization WMDA.
So, what can be considered as critical points and challenges of the CDSS development? Is it assessment of users requirements, CDSS development management, interdisciplinary cooperation among professionals, establishing the use of the CDSS, utilization of the CDSS applications and communication components, changes in methodologies for the health care organization, knowledge and model base correctness, decision support accuracy?
Each point can be critical, none of them can be neglected, and all must be coordinated with each other throughout the whole development process. Neglecting any of them could have fatal consequences for the entire project. The key is a common feedback from medical professionals to IT professionals and vice versa, to prevent misunderstanding. A communication link must be well-timed, i.e., development requires the involvement of medical professionals in the analytical team. Equally, the role of a coordinator with the deep domain knowledge and his communication with IT is crucial. In the case of the CDSS it is very difficult for a standard system analyst to gain this knowledge. For successful CDSS development, mainly for reasons of efficiency, it is important to use agile methodologies. Agility by itself does not solve the lack of knowledge but a coordinator knowledgeable in those methodologies and the medical domain can streamline the development process of CDSS.
New methods and the necessary decision-making models required for model-driven part of the CDSS are not often developed by medical professionals but by analytical professionals. Involvement of physicians within the validation of these methods and models is necessary. However, the willingness of medical professionals to make changes in operations and operating procedures with regard to the involvement of IS to these procedures plays also a significant role. It can therefore be concluded that the basis for a successful CDSS development is given by medical-(researcher)-IT communication and its well-built management.

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References

1. Berner, E.S., La Lande, T.J.: Overview of Clinical Decision Support Systems. In: Berner, E.S. (ed.) Clinical Decision Support Systems - Theory and Practice, pp. 3-22. Springer, New York (2007)
2. Georgiev, D., Houdová, L., Fetter, M., Jindra, P.: A Scalable Method for Efficient Stem Cell Donor HLA Genotype Match Determination. In: Energy, Environment, Biology and Biomedicine, Proceedings of the 2014 International Conference on Biology and Biomedicine II, pp. 28-32. INASE, Prague (2014)
3. HLA Nomenclature in WMDA file format – details of current HLA alleles and where known their unambiguous, possible or assumed serologically equivalent antigens. http://hla.alleles.org/wmda/rel_dna_ser.txt. Accessed April 13, 2016
4. Lee, S.J., Klein, J., Haagenson, M., Baxter-Lowe, L.A., Confer, D.L., Eapen, M., Fernandez-Vina, M., Flomenberg. N., Horowitz, M., Hurley, C.K, Noreen, H., Oudshoorn, M., Petersdorf, E., Setterholm, M., Spellman, S., Weisdorf, D., Williams, T.M., Anasetti, C.: High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation. Blood. 110(13), 4576-4583 (2007)
5. Moore, J.H., Chang, M.G.: Design of decision support systems. ACM SIGMIS Database - Selected papers on decision support systems from the 13th Hawaii International Conference on System Sciences. 12(1-2), 8-14, ACM, New York (1980)

6. NMDP allele codes. https://bioinformatics.bethematchclinical.org/hla-resources/allele-codes/. Accessed April 13, 2016
7. Nowak, J.: Role of HLA in hematopoietic SCT. Bone Marrow Transplant. 42(Suppl 2), 71-76 (2008)
8. Organisational Structure of CNMDR. http://www.kostnidren.cz/registry/1_organisational-structure.html. Accessed March 29, 2016
9. Power, D.J.:Web-Based and Model-Driven Decision Support Systems: Concepts and Issues. In: AMCIS 2000 Proceedings, pp. 352-355. AIS, Long Beach (2000)
10. World Marrow Donor Association International Standards for Unrelated Hematopoietic Stem Cell Donor registries (2014), https://www.wmda.info/images/pdf/20140101-STDC-WMDA_Standards_New_Housestyle.pdf. Accessed April 7, 2016