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RFID Technology in Preparation and Administration of Cytostatic Infusions

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1. Introduction

Cytostatics which are drugs used to treat oncologic diseases belong to very dangerous substances. These drugs often have very low therapeutic index, i.e. the difference between therapeutic and toxic dose is very low. Wrong dose can thus endanger the patient very easily. As these drugs are perilous also for the personnel who are handling them, Czech laws demand that the personnel concerned pass regular medical examinations. The number of shifts on sites where contact with cytostatics is possible has to be recorded. The laws order the record of basic information on preparation and administration of cytostatics; however, detailed monitoring of the drug in the course of the whole process is not required.

A state-owned medium-sized hospital with 200+ beds and more than 80 years of experience, Masaryk Memorial Cancer Institute highly specializes in the treatment of oncologic patients by surgery, chemotherapy and radiotherapy. The institute is focused on the treatment of solid tumours, which are in Czech environment represented mainly by breast cancer and colorectal cancer. For the treatment, the patients can be hospitalised, or, which is less expensive and has psychological benefit for the patient, receive their treatment at the outpatient clinic. Thus, the patient comes to the hospital, is checked by his/her physician, chemotherapy/radiotherapy is prescribed and administered/applied. On the same day, often just after a few hours, the patient is sent home.

In the pharmacy of Masaryk Memorial Cancer Institute (MMCI) we intended to implement a system that would be able to record who, where, when and how were exposed to cytostatics. Furthermore, we wanted to use the active support of preparation, i.e. introduce software that would help and navigate the personnel during the whole process, thus reducing the possibility of error. In the course of the project, we decided to include the outpatient clinic so as the administration of cytostatics could be recorded and supported, too. There are several ways to monitor the process and the possibilities of information technology can offer numerous solutions. In the end, radio-frequency identification (RFID) was chosen because it is more advantageous in some aspects than other systems.

1.1 Previous manner of prescription, preparation and administration of cytostatics

The process was standardised and consisted of several steps. The doctor prescribed the cytostatic infusions using hospital information system (HIS) and printed it in two copies, stamping and signing both of them. The prescription was a sheet of paper containing all days of the protocol and for each day individual lines with particular cytostatics and other

medications. In the case of outpatients, the patient had to carry one copy to the outpatient clinic, where he had his seat reserved, and one copy to the pharmacy. In the case of inpatients, the first copy stayed at the clinic, the second was carried to the pharmacy by anyone from the personnel. Chemotherapy was prepared according to the prescription, the prescription was signed by the personnel who prepared it, and returned to the clinic. The first copy was used as administration protocol at the clinic. The doctor was limited and could not prescribe any chemotherapy – the prescription was limited by diagnosis and only treatment protocols approved by the head of the clinic could have been used.

1.2 Critical points of the previous process

In the process, there were several critical points, where an error could have occurred. Because the pharmacy runs according to quality system and is regularly inspected and audited following EN ISO 9001:2008, no significant errors occurred. There were several control mechanisms, mainly based on the principle that the personnel watched each other and on strict adherence to standard operation procedures (SOPs). Thus, the change in preparation or patients was excluded. However, the person preparing the infusion could take the necessary volume twice and so accidentally double the dose. Such an error could not have been identified.

As the patients, or their relatives, had to carry the prescription to the pharmacy in person, and sometimes did not want other people to know they were treated by chemotherapy – the prescriptions were traditionally printed on yellow sheet of paper size A4 – they folded the prescription and put it away. Sometimes, they forgot to hand it over and they themselves were the reason why they had to wait for the administration for a long time.

In some cases, it was not possible to backtrack the batch number of used drug, which is important e.g. in the case of side effects. Since the drugs have limited stability after first use, this stability was recorded by dating the particular vial. If incorrect date was written on the vial, a drug of unwarranted quality might have been used.

The entrance of the personnel in the preparation room was recorded in written form. Making regular monthly or yearly sums was difficult and any erroneous record was practically impossible to find.

1.3 RFID technology in healthcare

RFID technology is based on the communication between a unique carrier of information, i.e. a RFID tag, and a suitable reader. This technology has recently found its use in healthcare (Lahtela & Hassinen, 2009; Lahtela & Saranto, 2009; Sun, Wang, Wu, 2008). Technical report prepared by RAND (Oranje-Nassau et. al. 2009) for the European Commission describes seven cases within the European Union. In one case, the project failed completely, in two cases, the RFID technology was replaced by another technology for economic reasons. It was these two cases, where RFID technology was used in hospital pharmacies to control the preparation and administration of drugs. One of these cases was the University hospital in Geneva (Spahni et al. 2006). The RAND report praises the technology as it can lead to increase in quality of healthcare; on the other hand, the report warns against its high costs. The costs are in case of RFID technology much higher than in other technologies, e.g. barcode or its derivatives.

RFID technology was used in hospital pharmacy also in Akita University Hospital in Japan. In the Czech Republic, RFID technology is used in three hospitals, in one case for

equipment, in one case for laundry and in our case for the control of preparation and administration of cytostatics. Another hospital announced its plan to introduce RFID identification in its management of blood and blood products.

2. RFID project at MMCI

2.1 Information systems
The preparation and administration of cytostatics is a matter of concern of three different information systems.

Hospital information system (HIS) contains all information on patients and their visits in hospital – reports, laboratory results, records, etc. Concerning chemotherapy, HIS contains a list of all chemotherapy protocols that are or used to be approved by the management of the clinic and are based on published information. Protocols that are not in use any more are listed only for information and the doctor is not able to load them from the system. The doctor has to use particular protocol for allowed diagnosis only. Only minor changes in protocol are possible: the dose of the cytostatic drug can be reduced (the reason has to be recorded), auxiliary therapy – antiemetics, antihistaminics, ions, liquids, growth factors – can be added or modified, and the days of the protocol can be moved slightly forward or backward.

Pharmacy information system (PIS) is standard software used in Czech and Slovak pharmacies. In this case, it is modified by adding new modules, e.g. the active support of preparation or personnel entry monitoring. Both HIS (GreyFox) and PIS (Medea) are products of Stapro, a Czech software company specialising in healthcare software.

Information system for administration of cytostatics (AIS) that is used in the outpatient clinic, and in the future possibly in the inpatient clinic, was developed solely for this purpose by IBM.

This three information systems exchange and store information allowing its backtracking or control. All three information systems are also available as "testing versions", which are used for training purposes and development of new functionalities.

2.2 General communication flow
Within the system, three different information systems communicate with each other and are connected by the means of a service bus as shown in Figure 1.

HIS (blue colour) is connected with Relational Database Management System (RDBMS) and communicates through APP Server with the service bus. The communication follows the JMS/XML format.

PIS (yellow colour) has three key modules: personnel entry evidence, storage evidence and active support of preparation. It is connected with RDBMS and communicates through APP Server with the service bus. The communication follows the JMS/XML format.

AIS (violet colour) communicates with the service bus in HTTP/SOAP/WSDL format.

2.3 RFID tags
The system is based on passive RFID tags, ISO standard 15693, working frequency 13.56 MHz. These tags are used in three different forms.

• adhesive labels for the vials, 31.5 mm x 16.5 mm
• adhesive labels for the infusion bags, 55 mm x 75 mm, on which RFID printer prints further information
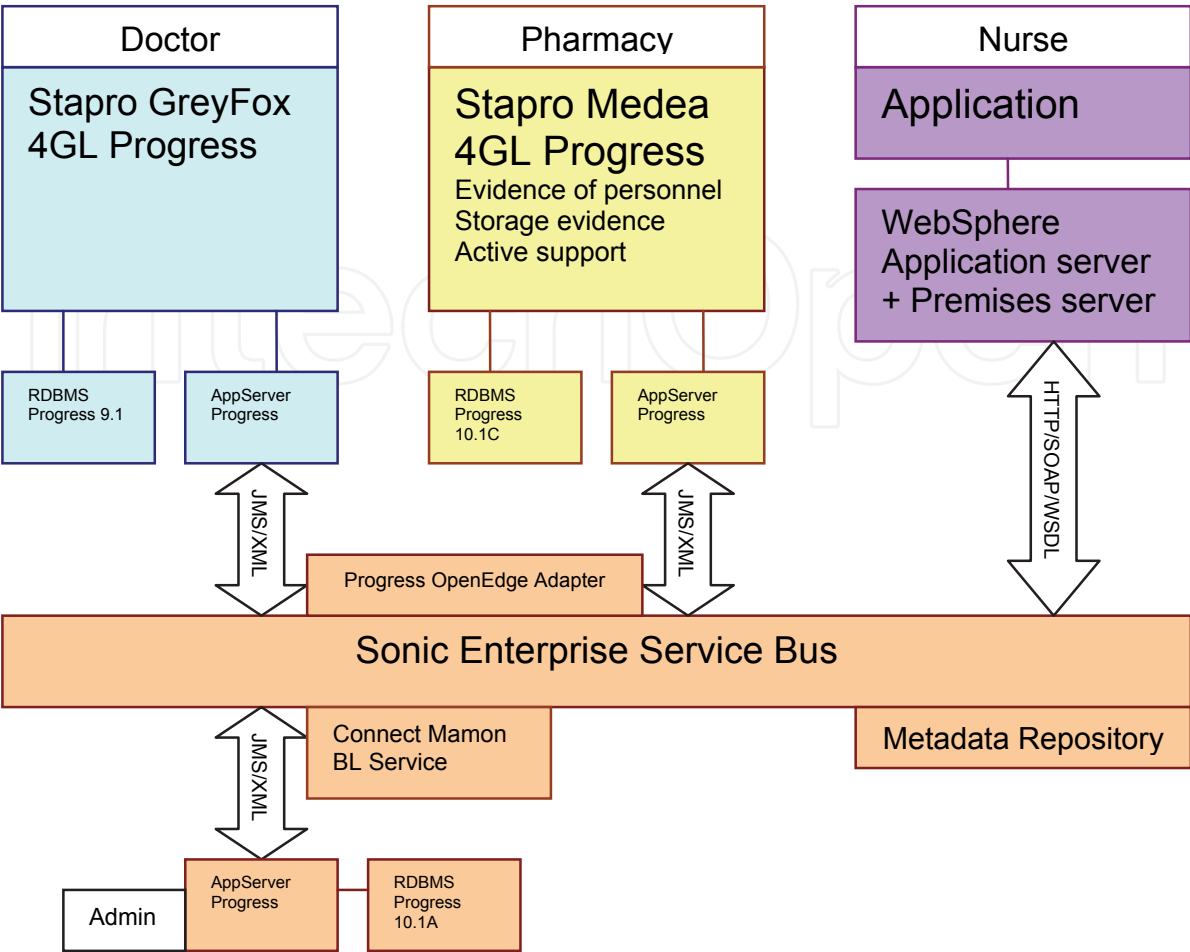• plastic ID cards.

Fig. 1. General communication flow.

In the course of the project, tags of other standards, e.g. I-CODE, and other working frequencies were tested. We supposed that the evidence of personnel would be based on rings with RFID tags identified by a frame with RFID reader working with UHF frequency. This idea was abandoned. The system used now may require higher activity on the side of the personnel, on the other hand, it is clear whether the personnel is entering or leaving the room, or just checking if the reader is functional. The personnel can clearly see if their entry was recorded correctly or who is inside the preparation room without actually having to go and have a look.

For several months, the vials were labelled by ARIO-SDM70 nano-tags, which was just a tag with a small antenna covered by an adhesive. The small size of the antenna was disadvantage, as the tag and the reader had to be in close contact and in correct position, which might have been tedious. Furthermore, the small size itself made it often difficult to find the tag on the vial at all.

Even though there is evidence (Erdem et al., 2009) that interference between the tag and the infusion bag is possible because the inside of the bag is conductive we did not meet such a case. We do not have any problems with interference between RFID tags and medical equipment (infusion pumps) either. Such interferences are known with other frequencies than 13.56 MHz (van der Togt et al., 2008). In Japan, there is the shortest allowed distance between a 13.56 MHz tag and medical equipment – 22 cm; however, testing showed that the

risk is significant in high-output antennas only. Actually, these are not used very often (Hanada & Horigome, 2008).

2.4 Technical solution – pharmacy

Figure 2 shows a simplified ground plan of the pharmacy. Turquoise colour corresponds to clean area class A, blue colour clean rooms class C. Light blue colour indicates material and personnel entrance hatches with material/personnel flow direction indicated by arrows. Red squares stand for RFID readers on the premises. Preparation room 1 is purposed for cytostatics, preparation room 2 for auxiliary medications.

The core of the system is a standard WLAN network, to which a service bus is connected. The network connects standard PCs in the Storage, in the small storage beside Preparation room 2, in Goods Intake room and in Completion room. These PCs are equipped with dial readers (RFID + barcode). In personnel entry, there is a small tablet PC with fixed RFID reader. In Preparation room 1, there are three isolators. An isolator is a special box, in which there is clean area Class A inside, their front side has two arms with gloves through which the personnel works. The backside of isolator is equipped with a touch screen and fixed RFID reader. The PCs themselves are positioned outside the preparation room, where they are easily accessible and not exposed to aggressive disinfectants. In Preparation room 1, there is also an industrial PC and a printer with RFID module. The printer is put in a pressure box where it is protected from disinfectants. In the pharmacy, there is also other necessary equipment, e.g. barcode printers. The system of work requires that RFID reader, industrial PC and RFID printer have to be available in at least two specimens. In case of maintenance or fault any equipment can be replaced immediately. There are three isolators, only two of which are in use, the third one is a reserve.
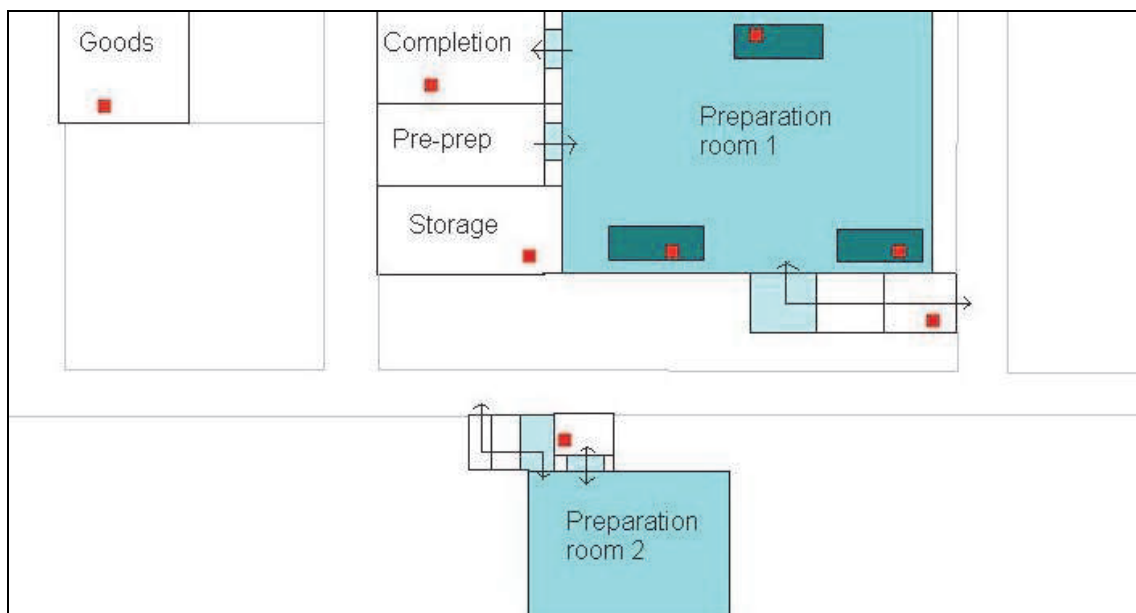

Fig. 2. Simplified ground plan of the pharmacy

2.4.1 Communication flow

RFID reader is connected with the PC through USB port that behaves as a serial port. RFID agent takes over the data by the means of RFID adapter and via a Message Queue (MQ)

client sends the message to the Premises Server, where the data go through App Server (via Message Driven Bean, MDB) and are sent by the means of Sonic MQ to the service bus.

Initially, RFID readers were connected by the means of Premises server. This solution was not fully reliable and in final solution is used in one case only. The readers are now connected through an USB port directly to the PC with the running application (Stapro MEDEA).

2.4.2 Readers

RFID reader reads the identification number (electronic product code, EPC) from the RFID tag. Obtained information is transferred along an USB connection to a PC, where it is processed further. In the course of the project, four different types of RFID readers were tested and used.

RightTag reader was initially used in the completion room where it was connected to a tablet PC. This reader reads RFID tags only. Because the completion process requires the use of both RFID tags and barcodes, this reader is now not used.

TagSys reader was placed initially in the room between Good Intake Room and the Storage; in these two rooms, there were reading frames connected to the reader via a coaxial cable. The reader itself was connected with the PC by a WiFi connection. Even though it was possible to work with one reader in two rooms, it was not possible at the same time. As there is neither visual nor audio possibility to communicate between both rooms and the WiFi connection was not reliable, we do not use this reader any more. Later, the whole hospital was covered by WiFi and so there was not any interference.
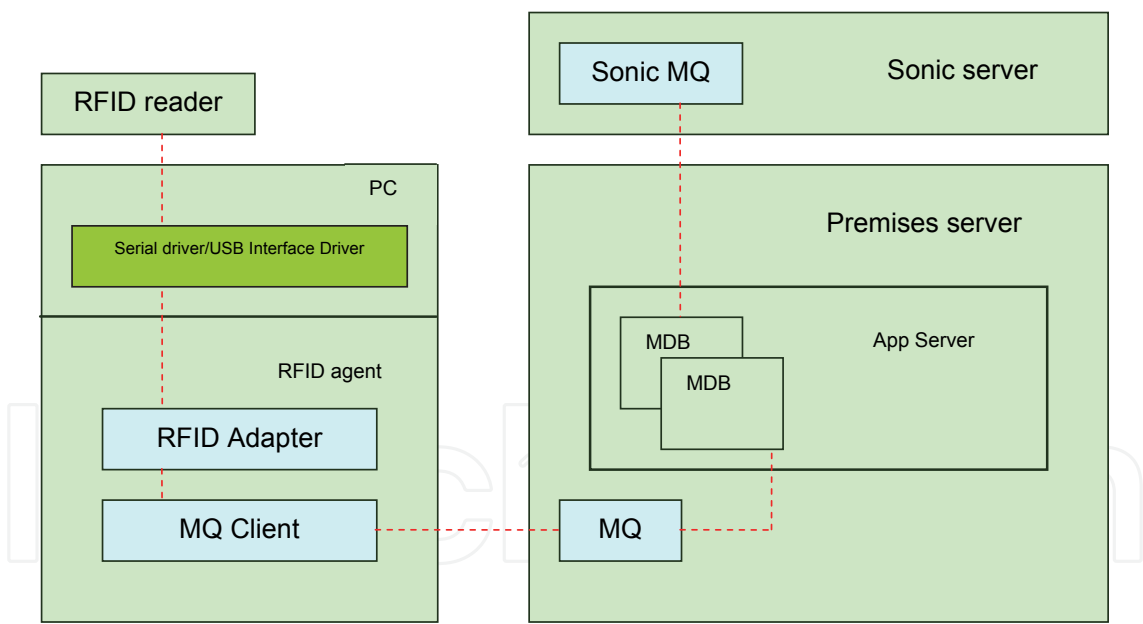
Fig. 3. Pharmacy. Communication flow

ACG readers are placed on goods intake, in personnel entry and in isolators. In the first two cases, the reader is connected with adjacent PC through an USB port. Should the reader or tablet PC in personnel entry break down (such a case happened) the particular part of the application can be run on the PC in the room of goods intake. In the isolators, the readers are placed in special covers that protect them from disinfectants and that are glued on the backside of the isolator. These readers are connected to particular PCs via an USB port (for details see chapter 2.4.7).

CPT8000 reader is a dual reader, working with both RFID tags and barcodes. These readers are used in the storage (RFID), auxiliary medication storage (barcode), and completion room (RFID+barcode). These readers are used also on other sites within the pharmacy.

2.4.3 RFID printer
In the preparation room, there is a printer SATO CL408E with RFID module. We use self-adhesive labels with in red pre-printed warning *cytotoxic substance*. The RFID tag itself is glued to the underside of the label. The printer couples the information on the preparation with the RFID tag and receives a confirmation that the coupling was successful. Only then is the label marked as usable. If the coupling fails, a new label has to be printed. The printer has to be protected from disinfectants and therefore it is placed in a special custom made pressure box. Next to the printer, there is an industrial compact PC with touch screen, which is used to run the application controlling the printing of RFID labels, a sub-module of the active support. The printer used to be connected with the computer though WiFi but after several months, this connection was replaced with standard Ethernet, which proved to be more stable and reliable.

2.4.4 Serial driver/USB driver
This driver serves the RFID reader on a low level and forms a virtual COM port, through which the communication with the RFID reader is channelled.

2.4.5 RFID agent and premises server
Console application serves the RFID reader and communicates with RFID Premises Server. Initialising and configuring when the RFID reader is switched on, RFID agent converts the protocols from RFID readers into the form of standardised messages. It shows up as an icon in the status area of the task-bar (green rectangle if running correctly, otherwise yellow or red).
Premises Server is a server application and connects communication buses IBM MQ and Sonic MQ. Each reading corresponds to one record in this format: *[2/26/09 15:31:34:734 CET] 00000027 SystemOut   O EventTagMDBean CONSUMED MESSAGE: null*

2.4.6 Communication protocol
The protocol manages the transfer of information on the EPC of a RFID tag from the reader to the service bus SonicMQ, where it is picked up by the HIS for further processing. The message contains information listed in Table 1.
The protocol contains other types of messages that enable the beginning and the end of the reading process at particular location and find out the status of reading location. These types are not in use at present.

2.4.7 Connection of isolators
Technology in isolators is connected with particular PCs that serve it by the means of USB/Ethernet converter. This method was chosen as the distance between an isolator and its PC is as much as 8 m. Such a distance can't be bridged reliably by a mere USB cable.
In isolators 1 and 2, the LCD touch screen is connected via a VGA cable with the PC. LCD touch screen and RFID reader are connected with the PC through USB cable, USB/Ethernet converter and switch. The switch is connected by Ethernet with an IP Watchdog.

Tag Message – TagEvent	
Published to	MOU.RFID.Event.Tag
Message Property	**Value**
RFIDEvent	TagEvent
RFIDEpc	EPC, e.g.: E07576576576AD
RFIDLocation	Name of the location, e.g.: Sklad.Cyto.Reader.1 *(Reader in Storage room)*
RFIDTagType	Type of the Tag, now only ISO15693 tags are used
RFIDTimestamp	In the format used byMQ

Table 1. Tag event

In isolator 3, the LCD touch screen is connected with the PC via a VGA cable as well as via a serial port, Ethernet and switch. The RFID reader is connected with the PC via an USB cable, converter, and switch. The switch is connected by Ethernet with an IP Watchdog.

The conversion from USB to Ethernet is managed by UBox2. This device enables the prolongation of USB through a LAN local computer network (Ethernet, Internet). USB-connected devices at the UBOX are accessible for more users at the same time. In contrast with traditional USB cable, the UBOX connection is not limited by the distance from the PC. Two USB devices can be connected at the same time (full-speed 12 Mbps). The energy supply of the USB device is standard (up to 500 mA for each device). UBOX ports appear in the operating system among other USB ports; however, they are only *virtual USB* ports, redirected to the UBOX port.

IP Watchdog GIOM 1200 is an automatically controlled socket which behaves according to user-defined rules. The socket can be used to switch on and off various devices, watch IP devices, reset servers, etc. In our case, the Watchdog is used to watch automatically if the communication is running correctly.

2.4.8 Software solution

Technologically, the solution is based on the integration of applications from two information systems that were already in use at MMCI. This software was modified or newly developed to suit the new demands. Following applications have to be changed:

StaproMEDEA Logistcics – pharmacy information system that manages complex logistics of drugs, or other stored commodities. Based on the demands of the project, the system was updated with a module using RFID identification of drugs, a module using RFID identification of personnel and a module supporting the preparation of cytostatics. Electronic communication with other systems was modified and improved, too.

StaproGreyFox – hospital information system supporting many inpatient and outpatient processes. Based on the demands of the project, the whole chemotherapy module was transformed. The medication is now supported more effectively and the communication with adjacent systems is improved. The system represents a sole information system that enables the doctor to have access to all necessary information without a need to search in other systems.

All communication XMLs have the main element named "chemo". This can have different attributes, in which the particular XMLs differ.

The receiving of XML have to be confirmed by the other side. If the "return" value equals "OK", the communication happened correctly. If the "return" value differs from "OK", an error occurred and the user is informed.

2.5 Technical solution – outpatient clinic

The outpatient clinic is used by those patients, who only visit the doctor, prescribed intravenous chemotherapy is administered to them and they go home, spending only several hours in the hospital. This is repeated for all the days of their chemotherapeutic cycle. Outpatient clinics are more convenient for several reasons but two of them are prominent. Firstly, such a system of care is much cheaper than standard care when the patient spends in the hospital several days. The second reason is psychological as a short visit in hospital does not stress the patient so much as a long stay.

RFID support of the administration at the outpatient clinic is processed through the co-operation of several components. These are HIS, PIS, PDAs used by the outpatient clinic nurses and the application in these PDAs, and the application on the Premises Server that communicates both with the PDAs and the HIS.

2.5.1 Hardware

Premises Server components and the HIS communicate with each other by the means of message exchange through MQ bus. This is the only possible way of communication between these components. PDA Sockets SoMo650 are used, the CF (Compact Flash) RFID reader for PDA is inserted in a slot in the PDA. In the outpatient clinic, there is also a WiFi access point LinkSys WRV200. The number of used PDAs is equal to the number of used seats.

Outside the outpatient clinic, there is an application running on IBM Premises Server that is placed in the server room of MMCI. This application holds status information on running application programmes and enables the users to use any PDA for particular record of administered dose. Thus, the PDA do not contain any long-term status information or any data on the patient or his/her application programme. The architecture has three levels and PDAs represent pure presentation level.

PDAs are used by nurse to record the steps taken when administering each drug to the patient. PDA serves as a tool to read the identificators – RFID tags and barcodes – and guides the nurse through the process of drug administration, using graphic user interface. PDAs communicate through a coded wireless network with IBM Premises Server where the server part of the application is run.

The WiFi access point is located in the nurses' room at the outpatient clinic. PDAs are placed at the door to the nurses' room in their chargers. When the nurse is going to administer a dose, she picks up the PDA from the charger and when working with the patient she has the PDA at her person. When returning to the nurses' room, she puts the PDA back to the charger. Because the PDAs are expensive and there are a lot of people coming in and going out of the outpatient clinic, a safety frame was installed at the door to the clinic. The communication is protected by the means of WPA-PSK (Wi-Fi protected access pre-shared key) and set rules at the MMCI's firewall.

2.5.2 Communication flow

The communication flow at the outpatient clinic follows the scheme pictured in Figure 4. The piece of information is read by the RFID reader, via its driver the information is send to

the PDA and on the presentation level it is sent to Premises Server. Premises Server (WebSphere Sensor Events) is a middleware mediating the communication between RFID readers and Sonic ESB. Premises Server is connected to Sonic data bus, through which the information is sent to the HIS. WebSphere application server is an application server, on which the server part of application is run.
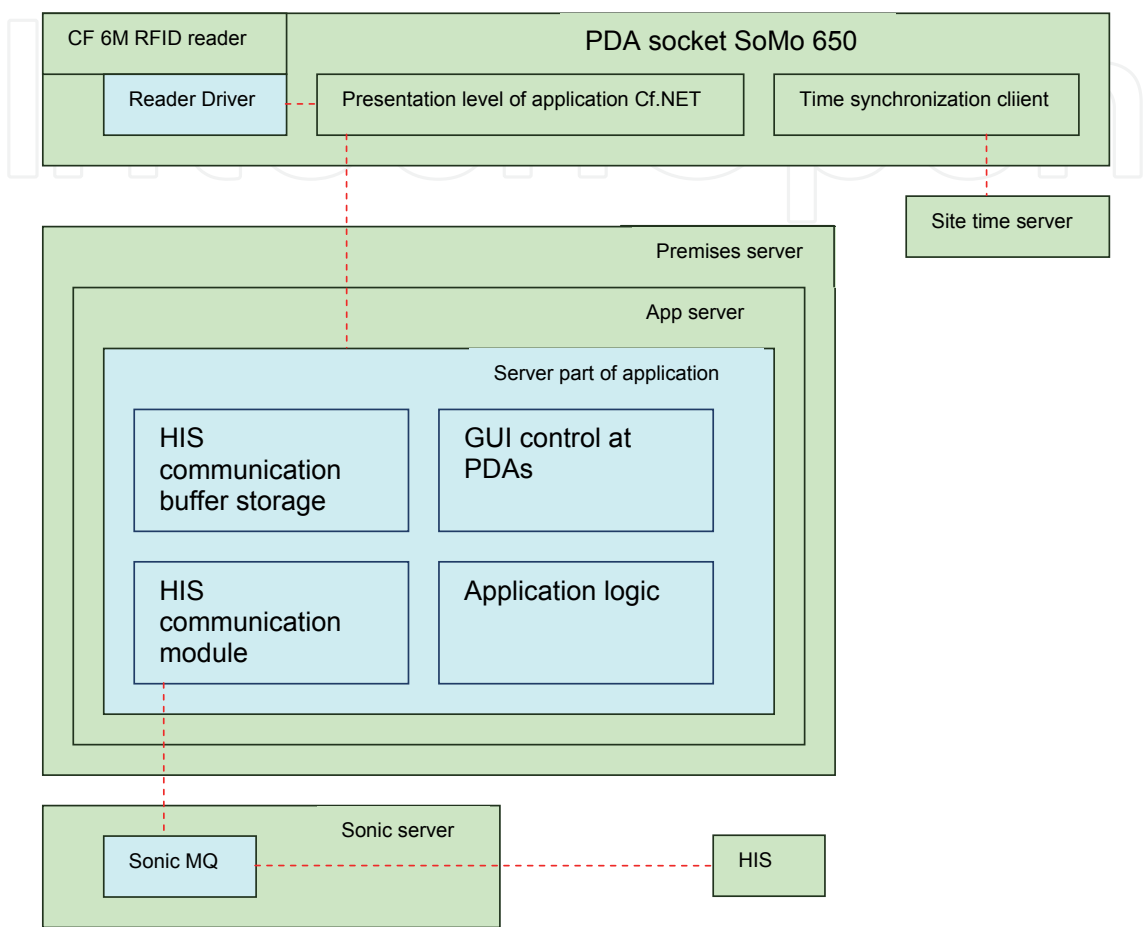

Fig. 4. Outpatient clinic: Communication flow. (MQ = message queue, GUI = graphical user interface)

Examples of communication between HIS and AIS are shown in Table 2.

Name	Direction	Queue	Structure
Query	AIS → HIS	MOU.RFID. Stacionar.doNIS	dotaz
Answer	HIS → AIS	MOU.RFID. Stacionar.doNIS	odpoved
Administration programme	HIS → AIS	MOU.RFID. Stacionar.zNIS	program
Administration protocol	AIS → HIS	MOU.RFID. Stacionar.doNIS	aplikace

Table 2.

2.5.3 Software
The application in the PDAs support the process of administration of cytostatic and auxiliary drugs. The application uses information on the patient and prescribed drugs that it

receives from the HIS. This information is used to check the process of administration. The application was developed solely for this purpose.

2.6 Evidence of personnel

On the entrance to the preparation room, the personnel have to identify themselves with their personal RFID ID card. In this way, the evidence of personnel who prepare cytostatic drugs is recorded. Obtained data are exported monthly and stored in defined folder where they are accessible for internal and external audits. The number of entries as well as their total length is recorded. The former meets the requirements ordered by the law; the latter is more quantitative and can be better related to any incidence of industrial disease. There is also another important quantitative value – the number of preparations per each person that shows direct participation in the preparation process and not only the presence in the room. Figure 5 shows the number of preparations for individual employees in 2010.
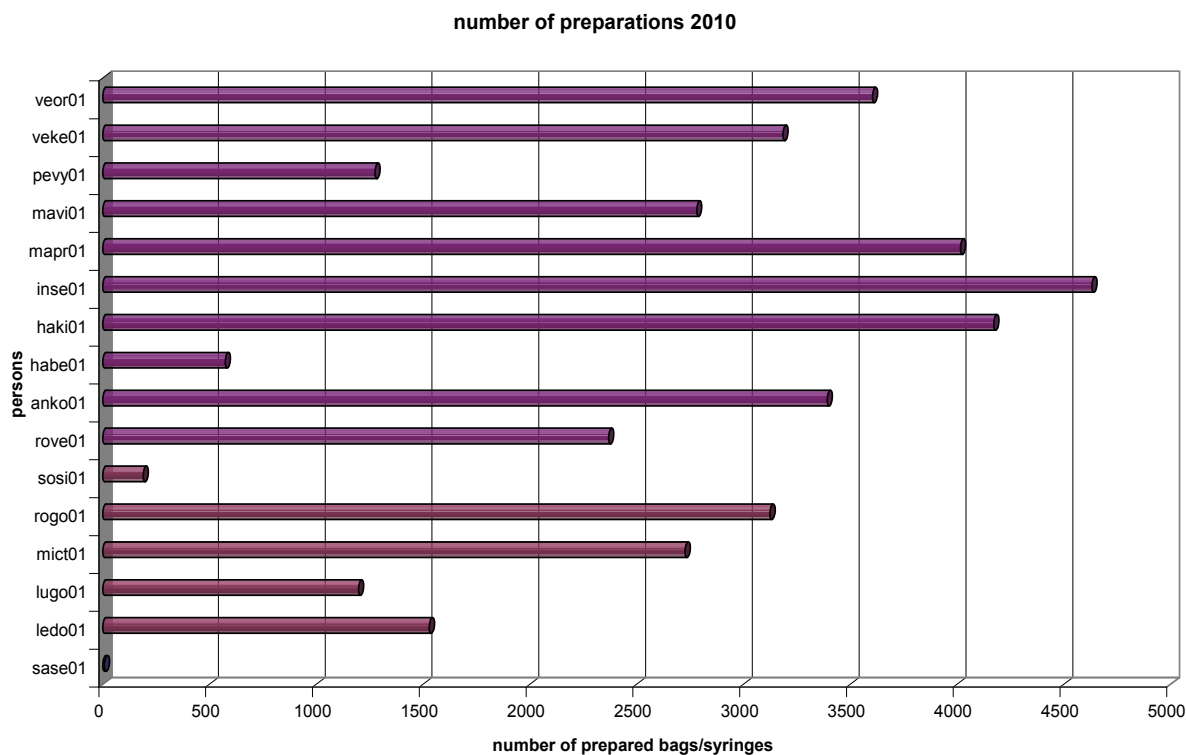

Fig. 5. Number of preparations. Employees with university degree in red colour, technicians in violet.

2.7 Preparation of chemotherapy
2.7.1 Entry of goods

When goods arrive at the pharmacy, they are put in the entry room where they have to stay until the entry of goods is finished. Cytostatic drugs can't be moved to the storage sooner than all vials are labelled with RFID tags. The tag with its antenna has a form of self-adhesive label. The PIS couples particular RFID tag with information on the vial: name, strength, ATC code, batch number, expiry date, price, VAT, supplier, etc. In this way, unambiguous identification of each cytostatic vial is certain. Cytostatics can be moved

between storages or moved to a bill only following the rules of RFID identification and only with the use of the tags. There are several kinds of bills – preparation, move to other storage, return to supplier, stock-taking – and all of them demand the use of RFID identification.

2.7.2 Electronic prescription of cytostatics

The doctor creates the electronic prescription of cytostatics in the HIS. He/she selects the patient and for his/her diagnosis can choose only from the list of approved chemotherapeutical protocols. The protocols are approved by the head of the clinic and are based on published information only. The doctor has the possibility of some modifications in the protocol. The individual days of the protocol can be moved slightly forward or backward, e.g. to avoid the weekends. The dose of a cytostatic can be reduced or particular cytostatic completely removed from the protocol. Such a reduction or removal has to be justified (e.g. serious adverse event or side effect) and the reason recorded. Auxiliary medications (antiemetics, antihistaminics, ions, liquids, growth factors) can be added, removed, or changed freely. Auxiliary medications can also be used as separate prescriptions. The prescription has usually one to ten lines. If the protocol consists of more days, each day has its individual prescription. Then the prescription is signed electronically – either all days of the protocol at once or only the first day, e.g. when there is a high risk of an adverse event.

If day 1 of the prescription equals to the actual date, the prescription is sent immediately to the pharmacy. The doctor has 15 minutes to recall the prescription, e.g. if he/she receives some new information on the status of the patient and needs to cancel or modify the prescription. Only after this interval the prescription can be processed in the pharmacy (the prescription is visible during this interval). If the doctor wants to recall the prescription after this interval, it is possible but the pharmacy does not guarantee that the prescription was partially or completely processed (prepared drugs won't be administered to the patient but they will be charged to the clinic).

If day 1 of the prescription does not equal to the actual date, the signed prescription awaits the right date. In case of inpatients, the prescription is sent to the pharmacy automatically at 5:45 in the morning (configurable time). In case of outpatients, the patient has to come in person to the outpatient clinic and the nurse sends only then the prescription to the pharmacy. The prescription for the actual date can't be sent to the pharmacy when the pharmacy is closed unless permitted by the pharmacy.

2.7.3 Identification

The electronic prescription arrives in the pharmacy. The system records the receipt (reads the heading), divides the prescription into individual lines and after 15 minutes informs the user by increasing the number of received unprocessed lines on the taskbar where there are three numbers – cytostatic, auxiliary, unknown. The prescription is not a fully functional bill, it is just a prescription stored in the data structure as a heading carrying all information that arrived from the HIS. The heading also bridges all bills that are created later and belong to this prescription (at least one bill for each line of the prescription).

When the user sees that there are unprocessed lines, he/she double clicks the taskbar and thus the CytoEvidence window is opened. This window has three sub-windows. In window 1 the user processes the unprocessed lines, in window 2, all received lines are visible, in window 3, all bills related to received prescriptions are visible. Windows 2 and 3

can be used only for viewing. In window 1, each line is attributed a bill of material, i.e. list of material that is necessary for the preparation and will be charged automatically (infusion bags, infusion lines, syringes, stopper, needles, etc.). This attribution is done according to the ATC code (defines the active substance of the drug) of the line and the way of administration. The same drugs can be often administered in different ways – e.g. intravenous infusion or intramuscular bolus syringe; different ways of administration demand different bills of material. If the system is unable to find a bill of material, i.e. it is not able to recognize both the ATC and the way of administration, the line is listed as unknown and the whole preparation can't be processed until a new/correct bill of material is defined. The bills of material are defined in the code-list of the system and are divided to two categories: RC (cytostatics, follows RFID process) and RS (auxiliary, follows barcode process).
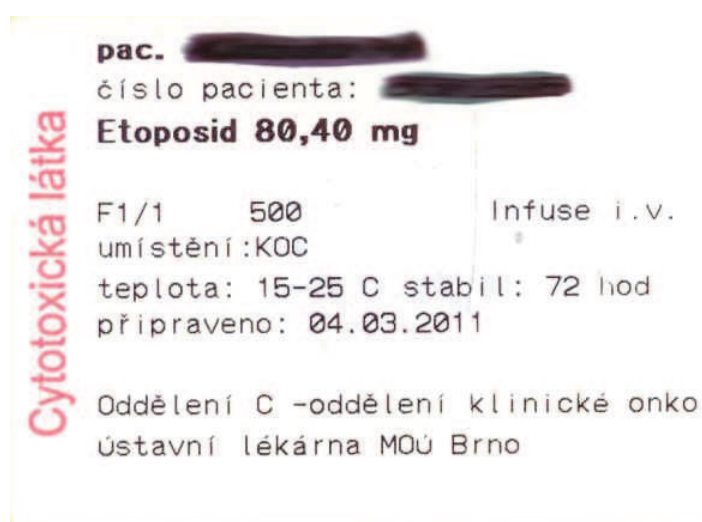

Fig. 6. RFID label used on the infusion bags (actual size).

Next step is the identification of the drug. Here, the system checks if the ATC code read from the vial is equal to the ATC code in the prescription. In cytostatics, RFID tag is read (identifying single vial), in auxiliary medications, barcode is read (identifying stock item). If the drug has not defined volume and amount of active substance that are necessary for the active support, the user is warned. After the identification, the user is allowed to print a label with all necessary information (name and ID of the patient, active substance and its dose, way of administration, medium and its volume, date of administration, + barcode in case of auxiliary medications). Vials, labels and all material necessary for the preparation are thoroughly disinfected and sent to the preparation room.

The system allows for the individual lines to be marked as priority, these appear in later stages of preparation in red colour and remind the users to process them as quickly as possible.

2.7.4 Preparation

The application "waiting room" is run on the computer with the RFID printer in the preparation room. When identified, individual lines are listed in the waiting room in order corresponding to the time when the prescription arrived in the pharmacy. The lines can be listed either according to surname of the patient or according to the ATC code. Both ways

can be convenient under certain circumstances. Lines, where RFID label was already printed but the preparation was not processed yet, remain in the waiting room and are in green colour. In such lines, the repeated printing of RFID label is possible, e.g. if the label was damaged before the preparation. Lines, which have been prepared but not completed yet, remain in waiting room, too, they are in grey colour and they can't be processed any more. In the application, the protocol can be viewed by the user if necessary.
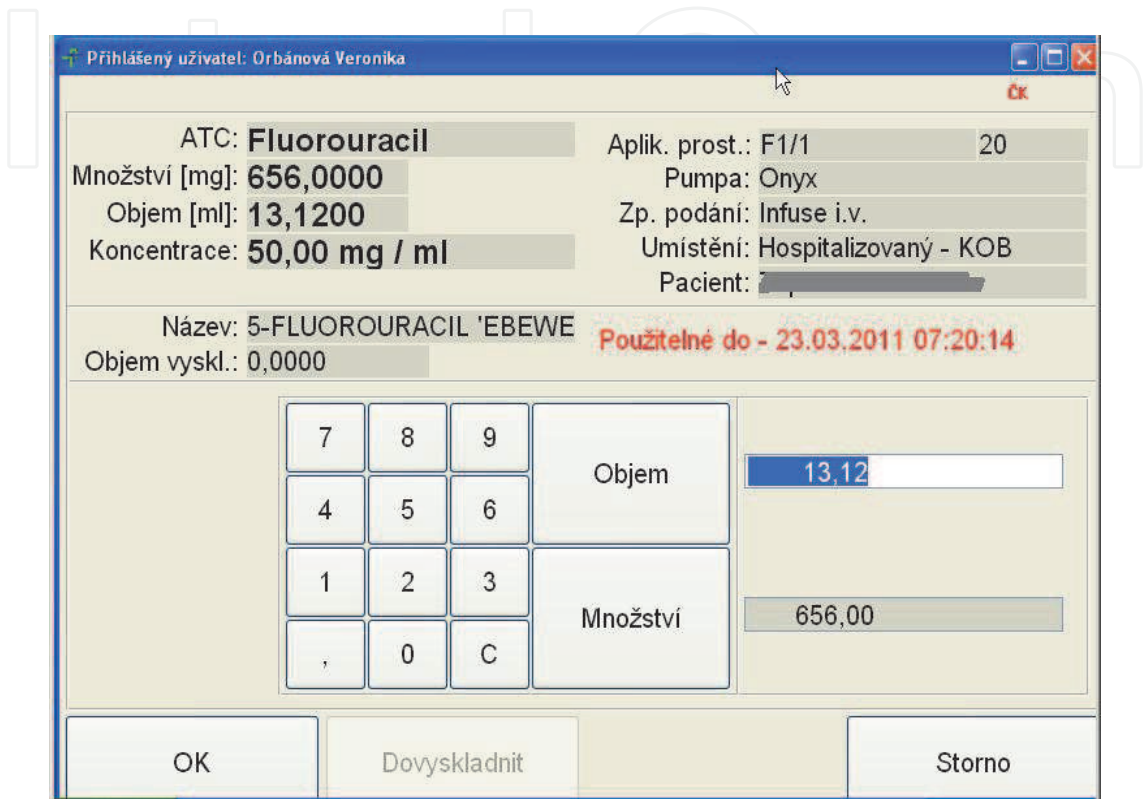

Fig. 7. Isolator. Vial window.

The user chooses a line and prints the RFID label (Figure 6.). Thus, the direct relation between the EPC of the tag on the label and the particular medication for particular patient is established. If the cytostatic is going to be administered in intravenous infusion, the RFID label is attached directly to the infusion bag. If the cytostatic is going to be administered as intravenous bolus, i.e. in a syringe, the RFID label is only put beside the necessary material. Because the syringes are too small, the label can't be used directly and is attached to the secondary packaging only. The label contains (from the top): identifiers of the patient – first name and surname, ID number, INN name of the drug and dose, used medium (here: saline) and its volume in ml, way of administration, location of the patient, temperature at which the bag has to be kept and its stability, date of the preparation, location where the medication was prescribed and the name of the pharmacy.

The user in the isolator identifies himself/herself (by his/her personal RFID ID card, time lock is configurable and set to 5 min, repeated identification is usually not necessary) and then reads the RFID label on the bag or the RFID label for the bolus. Then the user reads the first vial. The system automatically suggests necessary volume (either the full volume of the vial or a part of it). The user can change this volume according to actual volume found in the vial. This is important, as two significant cases occur naturally. Firstly, if the vial contains the precise volume of the drug and if the vial is used for more preparation,

losses can't be avoided and the last user is not able to find suggested volume in the vial. Secondly, some vials contain higher volume – as much as 105 % – and this volume can be used, of course. In both cases it is essential that the user puts in the system the actual volume that was taken from the vial. Then, the user takes further vials until required volume of the drug is taken.
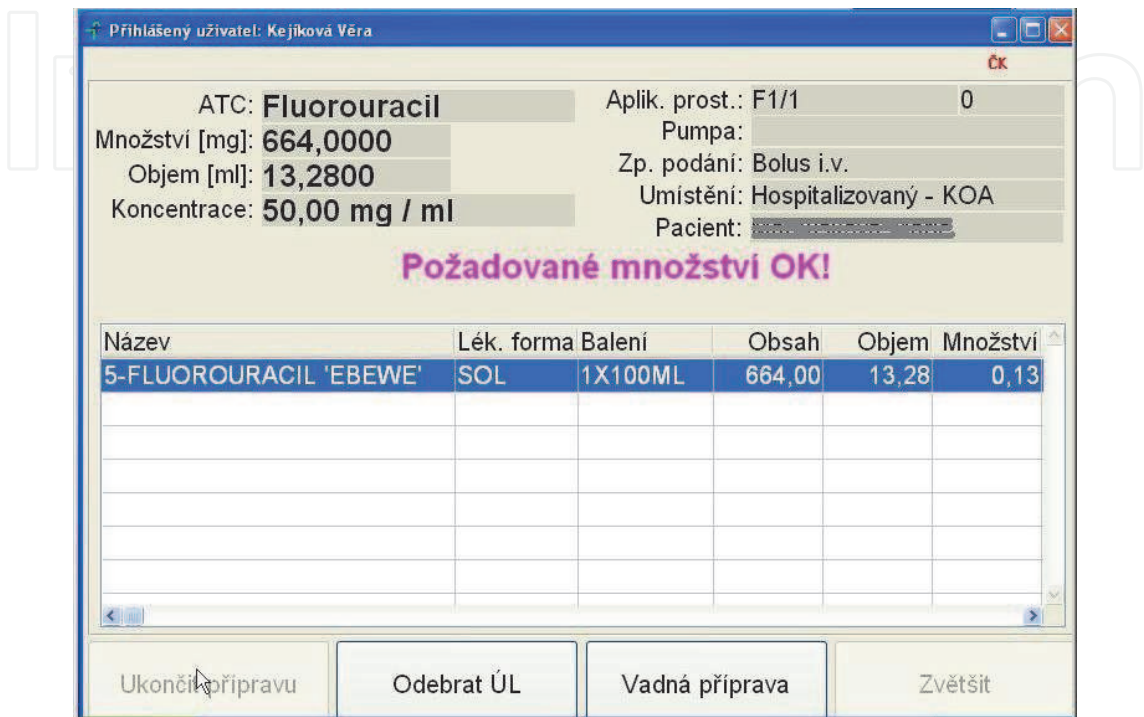

Fig. 8. Isolator. Preparation window

In figure 7 we can see the window as seen by the user in the isolator (the name of the user can be seen on top). In the top part of the screen, the user can see basic data on the preparation – INN name of the drug, dose, volume, concentration, medium (here: saline) and its volume (here: 20 ml), used pump, way of administration, location of the patient and his/her name. In the frame below, there is information on the used vial: name of the product, the volume that was already taken for the preparation (here: zero), and the date and time limiting the use of the vial. The dials serve for putting in of the volume that was taken (the input can be either volume or amount/dose). Buttons at the bottom are used to confirm that the step was finished or for return to previous step. In figure 8 we can see the moment when the preparation was just confirmed as finished. This windows lists in the tablet used vials and when the correct volume was taken, it enables the user to finish the preparation.

The system checks if the user takes the right drug (the ATC code on the vial has to the same as on the bag) and that the user does not take a drug whose stability after first opening has already expired. This stability has to be defined for each stock item and has to be watched because it not rare that the drugs containing the same active substance have significantly different stability after the opening. If the system recognizes the vial as past its usability it is charged to individual bill.

During the preparation, the system automatically creates particular bills (either a standard bill or an invoice) that contain used vials or their parts and material that is defined by the

bill of material. If the drug was stored in the Study-storage, two bills are formed, one for each storage. In clinical studies, the pharmacy sometimes uses own cytostatic drugs but these are not charged to the hospital, respectively to the health insurance company, but invoiced to the sponsor of the clinical study. This can be easily configured in the system.

When the infusions bags/syringes are prepared, they are sealed in a foil that acts as secondary packaging and first barrier in the case of an accident. In case of boluses, on this foil the user attaches the RFID label.

2.7.5 Completion

In the completion room the prepared infusion bags and syringes are controlled by another employee. All lines of the prescriptions are controlled here. The user reads the RFID label or barcode and visually checks that the preparation is not damaged, that there are not any leaks, etc. If everything is correct, the user confirms this fact in the system. If the last line was confirmed as checked the system suggests that the prescription should be completed. The message on completion is sent to the HIS. The completion has to processed also with prescription that was recalled after the limit and was at least partially prepared because the cycle has to be closed; in such a case no message is sent to the HIS.

2.7.6 Repeated use

In some cases, the preparation is not administered to the patient, usually because of sudden change in health status, e.g. allergic reaction. If the personnel at the clinic think it is possible to return the unused infusion bag to the pharmacy, it can be done. Firstly, the doctor or the nurse has to mark the bag as unused in the application programme in the HIS. The, the bag is carried back to the pharmacy. Here, the user in Cyto-storage room chooses suitable recipient – a line in the prescription that has identical ATC code and way of administration. Moreover, the dose has to be the same or higher than the dose of the returned bag, as the drug can be added to the bag but not removed. The user then couples the returned bag with the new preparation. This requires the user to identify himself/herself with RFID ID card. The stability of the returned has to be respected, too. However, it is not necessary to use the returned bag on the same day. The user now destroys the original labels on the bag and sends the bag with material, including more vials of the drug if necessary, to the preparation room.

In the preparation room, a standard RFID label is printed and attached to the old bag. Nevertheless, when the RFID label is read in the isolator, it already contains the drugs that are in the bag. If the dose is the same, the user just confirms that the preparation is finished, otherwise he/she adds required amount of the drug.

2.7.7 Repeated preparation

At most steps of the process, there is a risk of an accident and damage of the infusion bag. The bag can be dropped to the ground and burst, cut with sharp instruments, or, which is most frequent, the bag just leaks. In all cases, repeated preparation of the bag is necessary. Should the damage occur in the pharmacy, the user can mark the bag as damaged either in the isolator or in the completion room. Should the damage be found in the clinic, the nurse marks the bag as damaged in the HIS and the HIS sends a message to the PIS that the bag has to be prepared again. In all cases, the particular line of the prescription appears back in the CytoEvidence window. The whole cycle of preparation has to be processed again. Damaged bag can be charged either to the pharmacy or to the recipient.

2.8 Outpatient clinic

The administration of drugs is guided by application software that was developed solely for this purpose and is described in previous chapters. The steps that the nurse has to perform are described in Table 3. This process is repeated for each line (=medication) of the protocol.

Step	Process
1	The nurse reads her ID card with the PDA.
2	The system verifies the ID. If the ID is listed as nurse, the system shows information on this nurse (first name and surname).
3	The nurse reads the ID of the patient.
4	The system verifies the ID. If the ID is listed as patient, the system shows information on the patient (first name and surname) and asks the nurse to confirm the identity of the patient.
5	The system finds the actual application programme of the patient.
6	If there is not any actual application programme for the patient available, the system reports an error and returns to the Step 3, enabling the nurse to start working with another patient.
7	The system finds out if the patient had his/her blood pressure and pulse measured on that day. If yes, step 8 follows, if not, the nurse has to measure these values and put them in the application.
8	The system shows the actual application programme of the patient.
9	If the patient is in his/her first cycle and was not educated by the nurse, the nurse is asked to educate the patient and confirm the education in the system.
10	If the patient has in his application programme unconfirmed oral medications, these medications are listed one after another and have to be confirmed as the patient takes these medications.
11	The system finds out if an infusion pump, or two infusion pumps in case of parallel administration, is necessary for the administrations. If yes, the nurse has to identify an infusion pump. Identified infusion pump is shown on the screen.
12	The system finds out the actual status of the patient.
13	There are 4 possible statuses: Free, Drip, Pause, and Wait
13a	Free – the administration of the actual item of the application programme can be started. The system checks if the right dose is going to be administered.
13b	Drip – an item of the application programme is just being administered. The administration can be interrupted but the reason of the interruption has to be recorded (e.g. in case of a 3-hour infusion a visit to the toilet or a short walk).
13c	Pause – the administration was interrupted. The pause can be finished and the administration restarted.
13d	Wait – the administration of the item of the programme can be started only when the defined waiting time passes (e.g. some treatment protocols have necessary pause between two subsequent items).

Table 3. Administration of at the outpatient clinic

2.9 Further data

The system produces various data, as almost any operation is to some extent recorded. This enables retrospective control and traceability of who, when and how performed a particular

step. These data can be further processed and analysed and the results can be used to improve the process.

As example, the comparison of at which time the preparation is performed most frequently can be shown. The working time is divided in 4 shifts as shown in Figure 9. The amount of work is not divided evenly. Most preparations are processed in the morning. This is caused by three significant facts. Firstly, the prescriptions of inpatients, whose protocols cover several days, arrive in the pharmacy first thing in the morning. Secondly, the outpatients who come only for the administration and not for a check-up by their physician tend to come around 9 o'clock. Thirdly, the first wave of patients who come also for a visit at the physician have their blood results ready also around 9 o'clock. Therefore, most inpatients want their infusions to be prepared in a very short period, flooding both the pharmacy and the outpatient clinic with their requirements. An unwritten agreement between the pharmacy and the outpatient clinic states that the patient should wait for his medications one hour on average (including the 15-minute recall period reserved for the physician).
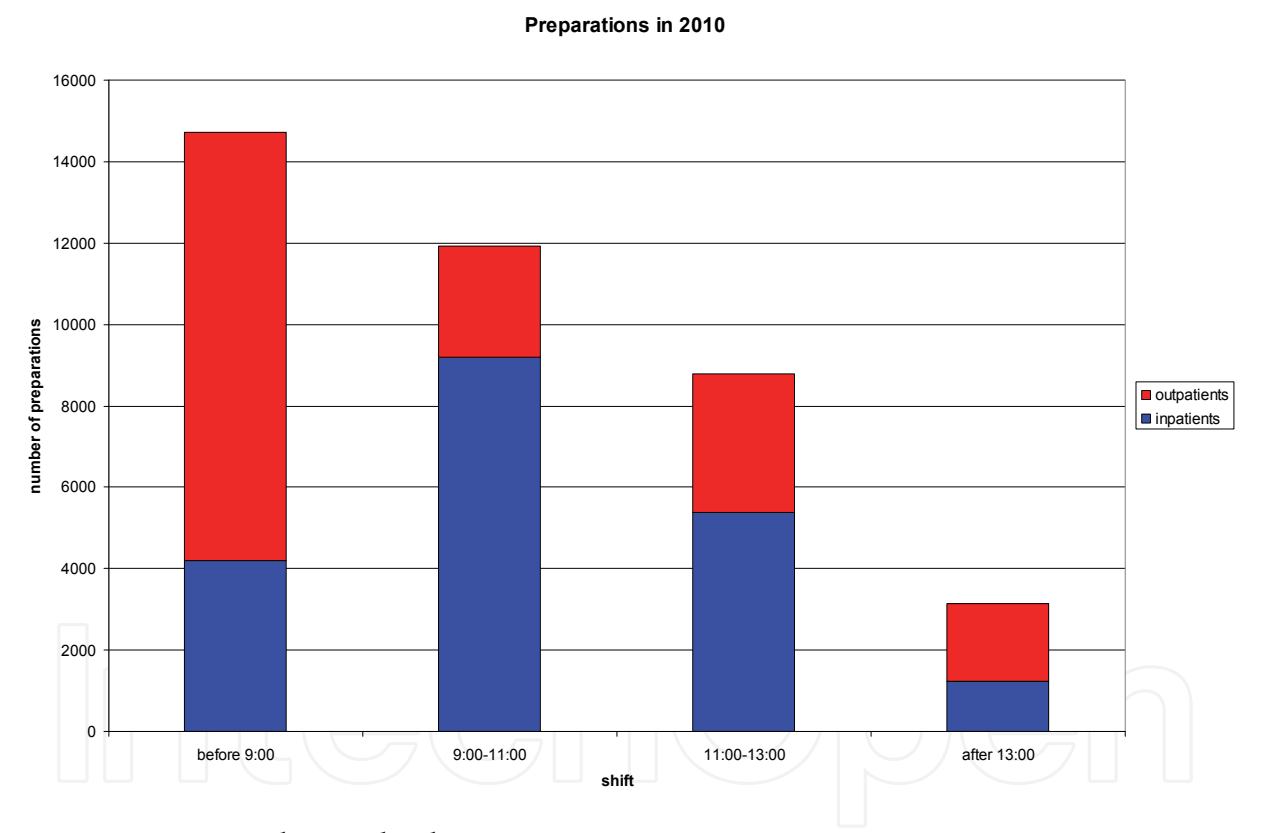

Fig. 9. Preparations during the day

In table 4, preparation times are compared. The value represents net preparation time in the isolator, i.e. between reading the RFID label and confirming the preparation as finished. The most frequent preparations in 2010 are listed, the lowest number of preparations in this set being 367 in bleomycin. The preparations were divided in three groups according to the amount of necessary steps. Group A lists preparations where the required amount is loaded in the syringe from the vial and then either the syringe is stoppered, or the content is first diluted with saline to required amount and then stoppered. Groups B and C include preparations that are administered in infusion bags. During the preparation, the infusion

line has to be connected to the infusion bag and prefilled with the medium, what increases significantly the time needed for the preparation. Group B includes preparations that are taken from the vial directly. Group C includes preparations that have to be first dissolved/diluted and only then they can be used.

Average and median times are very similar, SD is quite high. Once the content in the vial is dissolved, diluted or does not require such a treatment, the preparation time depends only on two physical factors – the volume that has to be taken and the viscosity of the solution. The data show how convenient it is when a preparation that used to be supplied as lyophilized powder or concentrate that had to be dissolved/diluted is suddenly available in dosage form for direct use. This is the case of topotecan in three last months of 2010. This fact is one of the causes why the data for topotecan are so low. The data show how inconvenient it is when only vials of low strength are available in the market. This is the cause of cetuximab exhibiting so high numbers in Group B. Cetuximab is available in 100mg strength only, requiring 4-10 vials for each preparation. On the other hand, the numbers for cisplatin and etoposide, which require 1-2 vials for the use, are low. However, in 2011, significant increase in cisplatin times is expected, as the product is now available in twice lower concentration – the volume that has to be taken is now twice so high.

Preparation	Average (min:s)	Median (min:s)	SD (min:s)	Number of preparations
Group A				
5-Fluorouracil bolus	1:03	0:57	0:36	4728
5-Fluorouracil onyx	1:04	0:58	0:37	3953
Vinblastin	1:46	1:29	1:10	631
Bleomycin	1:54	1:47	1:19	367
Group B				
Cisplatin	1:45	1:29	1:13	5009
Paclitaxel	2:40	2:32	1:08	2962
Cyclophosphamide	2:30	2:09	1:32	1900
Bevacizumab	2:34	2:34	1:06	1378
Etoposide	1:24	1:21	0:42	1305
Carboplatin	2:26	2:19	1:01	1196
Oxaliplatin	3:16	3:24	1:28	1090
Irinotecan	2:35	2:25	1:16	990
Doxorubicin	2:29	2:04	2:34	931
Epirubicin	2:50	2:48	0:54	925
Cetuximab	5:08	4:30	2:28	684
Panitumumab	3:21	3:07	1:58	397
Group C				
Trastuzumab	3:43	3:32	1:44	2357
Docetaxel	3:49	3:32	1:54	1146
Gemcitabin	4:17	4:11	1:54	1025
Topotecan	2:06	1:58	0:59	1004
Iphosphamide	3:50	3:09	2:54	687

Table 4. Preparation time

The table illustrates that the preparation time is 1-5 minutes. In the preparation of cytostatics, automated preparation performed by robots has been in the vogue recently. In spite of the fact that the producers of the robots promote them as extraordinarily convenient, the fastest robots need at least 5 minutes for each preparation. The robots decrease the human factor in the preparation but the benefit on the side of efficiency is still awaited as well as the patient waits until his medication is prepared.

3. Conclusion

The project was implemented in full run in October 2009. Neither erroneous preparation nor administration has been recorded. Within the Czech Republic, the RFID technology in preparation and administration of cytostatics is used solely at MMCI. It is an example of a multidisciplinary solution which was tailored to the needs of the MMCI. The goal was to reduce the human factor in the whole process.

The solution leaves two important challenges for the future. Firstly, the administration of cytostatic and auxiliary medication to the inpatients will be included, as well. Inpatients receive 40-50 % of preparations processed in the pharmacy. This will require minor investments in hardware and thorough education of nurses in inpatient clinics. Secondly, unless the prize of RFID tags decreases significantly in three years, we will be forced to adjust the system to another type of unique identificator. The system was developed to be suitable for unique identification in general and only some changes in hardware will be necessary.

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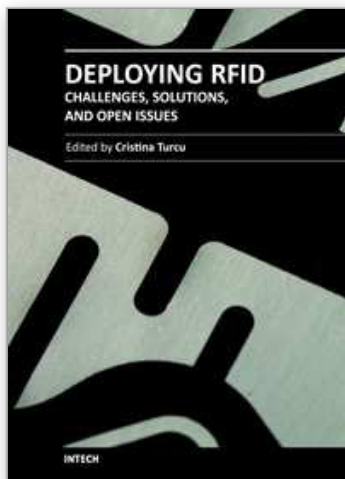
Deploying RFID - Challenges, Solutions, and Open Issues

Edited by Dr. Cristina Turcu

Radio frequency identification (RFID) is a technology that is rapidly gaining popularity due to its several benefits in a wide area of applications like inventory tracking, supply chain management, automated manufacturing, healthcare, etc. The benefits of implementing RFID technologies can be seen in terms of efficiency (increased speed in production, reduced shrinkage, lower error rates, improved asset tracking etc.) or effectiveness (services that companies provide to the customers). Leading to considerable operational and strategic benefits, RFID technology continues to bring new levels of intelligence and information, strengthening the experience of all participants in this research domain, and serving as a valuable authentication technology. We hope this book will be useful for engineers, researchers and industry personnel, and provide them with some new ideas to address current and future issues they might be facing.

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