



Research Article

The Development of a Software System for Patients with Breast Cancer Receiving Chemotherapy Treatment: A Pilot Study

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Abstract

Until recently, anti-cancer clinics in order to plan and schedule chemotherapy treatments applied time-consuming methods, characterized by a high risk of error occurrence. Considering all the barriers that make chemotherapy treatment and demanding procedure, to evaluate if a chemotherapy management program could improve the administration of chemotherapy treatments. The authors developed "Carci", a software tool designed to support anti-cancer clinics. The particular software program aims to provide an improved administration system for injectable anticancer agents and eliminate medication errors that could yield fatal events. The recording of patients' data, the selection of the appropriate treatment protocol, the calculations of drug dosages, the correct preparation and administration of injectable solutions and the updating of secretariat, were conducted both manually and by using the computerized method. These two methods were compared and contrasted. The use of "Carci" resulted in a decrease in the time required to calculate patients' Body Surface Area (BSA) and in a decrease in the occurrence of errors concerning the dosage of medication administered. A total of 18 patients with breast cancer were assigned to this pilot study. Significant differences were observed in BSA values ($p=0.0391$) and dosage ($p=0.0042$) between the computerized method "Carci" and manually by the doctor. Although this has been a pilot study, further evaluation of this software program in a larger sample of patients is required. Preliminary data, however, suggests that "Carci" can minimize the risk for error occurrence making chemotherapy treatment faster, easier and more accurate.

Keywords: Cancer, chemotherapy treatment, software program, treatment protocols.

Introduction

Chemotherapy is the process of using of chemical agents or medications to treat cancer. It is a systemic therapy that affects the whole body, since the action of chemotherapeutic agents is not limited to malignant tissue, but it also affects normal cells. Administration routes vary, including oral, intravenous, intraperitoneal administration or delivery via catheter. The severity of the side effects commonly depends on the agents used, the dosage, the duration of treatment and treatment cycles, on other accompanying drugs and the individual's response to received medication, as well as the patients' health status. However, it is vital that the agents are administered at a patient-appropriate dosage in order to yield optimal results and prevent adverse events due to toxicities¹. Dosage individualization is of significant importance, since it prevents toxicity due to overdose and avoids treatment failure due to inadequate drug administration^{2, 3}. The guidelines for the safe handling and the use of anticancer agents have been established by the National Institute of Health and the American Society of Hospital Pharmacists⁴.

Hospitals and clinics providing chemotherapy treatments face a number of problems on daily routine tasks, such as updating patients' records and operational problems concerning the overall organization of treatments and medication management. The time spent on defining the appropriate treatment protocols, calculating drug dosages and specifying their preparation instructions is usually long, and cuts down on health care professionals' productivity. Also, professionals from different departments who need to cooperate in order to provide optimal treatment, they usually lack immediate access to important information waiting for data to be collected from each department. Additionally, work overload does not allow doctors to be constantly up to date concerning new medications and chemotherapeutic agents, which may be improved or may be less expensive than old, outdated ones. An initial attempt was made by Okayasu *et al.* in 2009 in order to

minimize errors on the preparation of chemotherapy treatments by developing a computer-assisted biohazard safety cabinet enabling for the safe handling and preparation of the mixture⁵.

Aim of the Study

The purpose of the present pilot study is to present and describe "Carci", a software tool developed to meet the needs of anti-cancer clinics in improving the chemotherapy treatment procedures and in decreasing their operational cost.

Method

Technical Details of the Program

The software was developed in Visual C++ using Microsoft Visual Studio 2010. Minimum operating system requirements include Microsoft Windows XP, service pack 2. It is mandatory that each computer can be connected with an Ethernet network, wired or wireless. There are no requirements concerning the processor, but the computer must have at least 1 GB of RAM. To use the program in a system network, there must be a Server, for which there are no specific requirements, but the ability to install an SQL database. The network is recommended to be local, not allowing Internet access, in order to secure confidentiality.

Study Population

Data were recorded from 18 individuals, 17 females and 1 male. Recruitment took place at IASO Hospital of Athens, during a 6-month period. All patients were diagnosed with breast cancer.

The study was approved by the ethical committee of the hospital and conducted in compliance with the ethical principle of the Helsinki Declaration. All information regarding participants' clinical condition, medication and medical history were provided by the participants during their interview with the clinicians. Documents regarding medical tests and biochemical data were collected. Patients' characteristics are presented in Table 1.

Table 1: Demographic and Medical Characteristics of the Study Patients

Characteristics	n
Sex (male/Female)	1/17
Age (years)	54.72±12.34
BMI (kg/m ²)	29.4±5.8

Statistical Analysis

In order to investigate any potential difference between the therapeutic choices of the Doctors in charge and the automatic choices of the “Carci” software used, we performed a Wilcoxon non-parametric rank test for paired samples⁶, due to the fact that our data did not meet the normal distribution criteria based on a Jarque-Bera hypothesis test⁷. A p-value of <0.05 was considered significant for all our statistical analyses. All calculations have been performed using Matlab® R2007a Technical Software⁸.

Results

The support system “Carci” is comprised of two subsystems, “CarciMed” and “CarciWard”. “CarciMed” is the drug database and it is a separate entity to the patient database “CarciWard”. “CarciMed” provides the interface to set and configure the protocols and drugs available to the system. A system vendor called “the administrator” has access to “CarciMed” and is responsible for updating the database on a monthly basis. The administrator can alter and monitor all data with regard to the various treatment protocols, medications, method of administration, sequence and duration of administration of the chemotherapeutic agents.

Currently, only breast cancer chemotherapy treatments are supported, therefore only medicines and protocols relevant to that aim have been configured. More specifically, there are 19 protocols for complementary chemotherapy (adjuvant) and 5 for locally extended breast cancer (locally advanced treatment), according to the international guidelines⁹. The injectable chemotherapeutic agents that are present in these protocols and consequently exist in the database are 10^{10, 11}.

Biochemical factors and additional pathological conditions that may influence the dosage of administration of every chemotherapeutic agent are also taken into account in the “CarciMed” database. Additionally, “CarciMed” holds all relevant information regarding the recommended infusion method (IV push, IV infusion) and the compatibility of each solvent with each anticancer agent.

“CarciMed” is linked with “CarciWard”, the platform developed to support anti-cancer clinics. “CarciWard” provides a number of forms with patient-related information and each of them can be filled in by the Health Care Professionals within the hospital or the clinic. The clinic secretary is entitled to have access, make additions, deletions or modifications only in the form “PATIENT INFORMATION”. Doctors have access in all forms, apart from the one with “ADMINISTRATOR’S INFORMATION”. More specifically, they may view and intervene in the forms “PATIENT INFORMATION”, “DIAGNOSTIC INFORMATION”, “MEDICAL HISTORY” and “THERAPY PROTOCOL”. Nurses have access in two forms, “PATIENT INFORMATION” and “MEDICAL HISTORY”. Pharmacists have access in the form “THERAPY PROTOCOL” only, to which they cannot intervene. Health Care professionals from different departments are entitled to have selected access. The reasons behind the different access levels granted to the Health Care professionals are two-fold; the fact that unauthorized staff intervenes to patients’ data or treatments may be very dangerous for a patient’s health, since even the minor modification in a drug dosage may be fatal. Thus, access in the program is always named protocol, and dosage modifications always require doctor’s approval. The second reason is that the personal details of the patients should be kept confidential. This is accomplished by restricting view access, though, according to the work force credentials that are used;

the needed information for the accomplishment of the needed work tasks is provided.

“CarciWard” is comprised of **five electronic forms**; each of them has several subsections and fields to be filled in. Health Care Professionals have selected access to one or more of the forms, depending on their specialty. The “CarciWard” software administrator, which is usually the Head of the Clinic, has access to all of them. All, doctors, nurses, pharmacists, secretaries and the administrators may access the forms they are entitled to, searching for the information they need either by the date of a patient’s treatment or by the patient’s name.

The form “PATIENT INFORMATION” contains the patient’s personal information

(name, clinic, doctor in charge, insurance fund), contact information, non-cancer pharmaceutical treatment, allergies, date of birth, sex, height, weight, Body Surface Area (BSA) and appointment date (figure 1). The system has also a specific algorithm in order to automatically calculate the BSA of the patient, of each person, a factor that highly affects the dosage of the chemotherapeutic agents. The level of BSA is calculated based on the values given for height and weight¹². Patient’s personal information may be viewed once a patient’s name has been selected from the list that appears at the upper part of the form. Access to this form is permitted to clinic Health Care Professionals (doctors, pharmacists, nurses) and the clinic secretary.

The screenshot displays the 'CarciWard' software interface. At the top, there are search options for 'Treatment Date' and 'Name'. A dropdown menu shows a list of patients, with 'ASD AS [2378]' selected. Below this, there are input fields for 'Patient Surname' and 'Patient Name'. A checkbox labeled 'View Patients without Defined Treatment' is present. The main form is titled 'Patient Information' and is divided into three sections: 'Personal Information', 'Contact Information', and 'Medical History'. The 'Personal Information' section contains fields for Surname (ASD), Name (AS), Middle Name, Clinic (Anti-Carcinic), Doctor (K A), Patient Code (2378), Insurance Org. (Αγώοο), Birthdate (13/11/1972), Sex (Female), Height (234.00 cm), Weight (234.00 Kg), and BSA (3.81 m2). The 'Contact Information' section includes Address, Telephone (210456789), Mobile (691234567), and Fax. The 'Medical History' section includes Patient Medication (Minocin) and Allergies (None Identified). At the bottom right, there are buttons for 'Change', 'Remove', and 'Add Patient'. The top right corner shows 'Connected as: Administrator' and a 'Print All Tickets' button.

Figure 1: Patient Information form on CarciWard. In this Form, the Patient’s General Information is Recorded (Name, Surname, Date of Birth, Contact Information) Including also the Height, Weight and BSA of the Patient.

The form “DIAGNOSTIC INFORMATION” contains information about the status and the stage of cancer of the patient (figure 2). The doctor completes information about whether the patient has undergone surgery or lymph node dissection (in cases of breast cancer), defines the clinical stage of

cancer, the multiplication ratio and gives a final diagnosis. The doctor also defines the treatment protocol. In addition, old protocols appear in the form, so that the doctor can access the treatment record of a patient.

The screenshot shows the 'CarciWard' application window. At the top, there are search options for 'Treatment Date' and 'Name'. A dropdown menu is open, showing a list of patient names: 'ASD AS [2378]', 'Doe A. [1234]', 'J IOANNA [567]', 'qwerty qwerty [987564]', and 'X Y [9876]'. Below the search fields are input boxes for 'Patient Surname' and 'Patient Name', and a checkbox for 'View Patients without Defined Treatment'. The main area has several tabs: 'Patient Information', 'Diagnostic Information', 'Medical History', 'Therapy Protocol', and 'Administrator Information'. The 'Diagnostic Information' tab is active, showing a 'Patient Treatment' section with 'Current Treatments' and 'Previous Treatments' (Breast - BRAVT RAD - Paclitaxel - Transtu x 4). Below this are fields for 'Surgery', 'Dissection', 'Breast', 'Clinical Stage' (T, N, M), 'Estrogen receptor (ER)', 'Progesterone receptors (PR)', 'HER-2 overexpression' (IHC, FISH/CISH), 'Proliferation index Ki 67', and 'Diagnosis'. A 'Change Data' button is located at the bottom right of the form.

Figure 2: Diagnostic Information form on CarciWard. Information on Previous Surgeries, Dissection, Clinical Stage of the Patient, Estrogen and Progesterone Receptor and HER-2 Overexpression Values are Recorded.

The form “MEDICAL HISTORY” contains data on lab test results of the patient (figure 3).

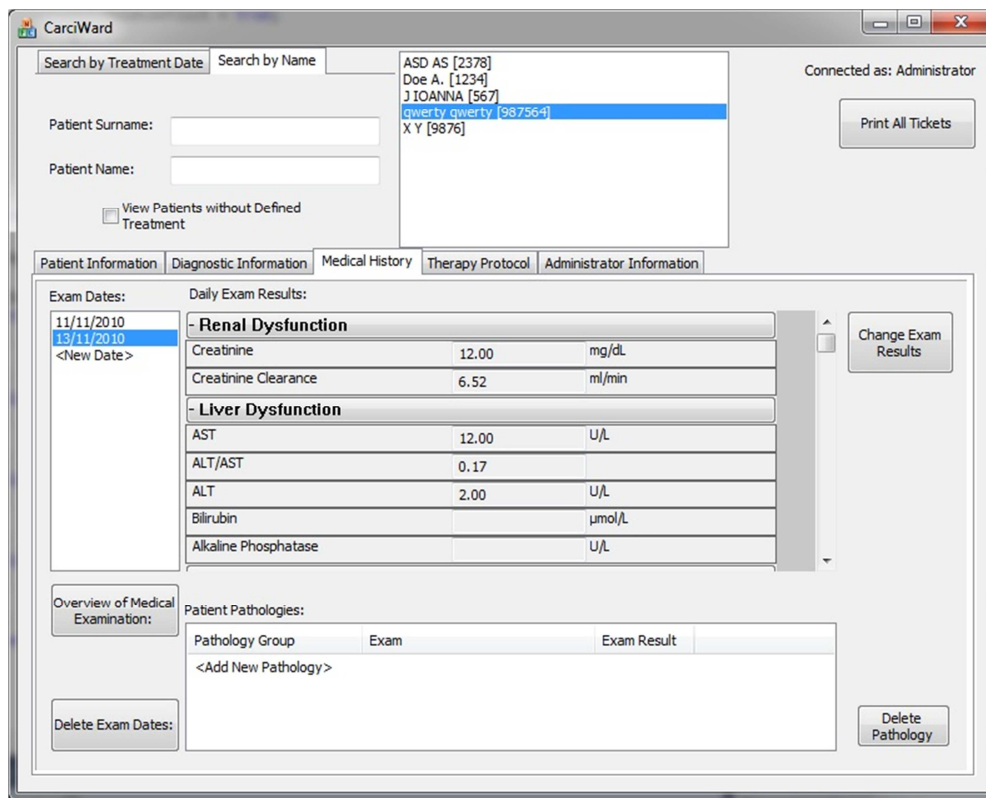


Figure 3: Medical History form on CarciWard. The Medical History of the Patient is Recorded on this Form, Such as the Degree of Renal and Liver Dysfunction Estimated through Various Factors on Blood Test

Test date is typed and lab test results such as kidney, liver and cardiac function, platelet and white blood cell count, serve as input data (Table 2).

Table 2: Shows the Biochemical Factors Needed to be Recorded on the “MEDICAL HISTORY” Form.

TEST	BIOCHEMICAL FACTOR MEASURED	MEASUREMENT UNIT
Renal Dysfunction Degree	Creatinine, Cr*	mg/dL
Renal Dysfunction Degree	Creatinine Clearance, ClCr	mL/min
Liver Dysfunction Degree	AST	U/L
Liver Dysfunction Degree	ALT/AST	
Liver Dysfunction Degree	ALT	U/L
Liver Dysfunction Degree	Bilirubin	µmol/L
Liver Dysfunction Degree	Alkaline Phosphatase	U/L
Blood Count	Platelets, PLT	$\times 10^9 /L$
Blood Count	Neutrophils, ANC	$\times 10^9 /L$
Cardiac Dysfunction	Left Ventricular Ejection Fraction, LVEF	%

In case where the lab test results indicate the presence of a co-existing clinical/pathological condition, the doctor needs to add the condition in the field "Patient's Pathologies". As pathologies, there have been listed Pathological Conditions/ Manifestations or/and Tests that take place during chemotherapy treatment and cannot be measured through a daily number value.

The pathologies that have been studied for this program and commonly alter the dosage of injectable chemotherapy agents are the following:

Blood Pathologies: Febrile Neutropenia, Intolerable Bone Pain

Neuropathies: Neurotoxicity, Peripheral Neuropathy

Renal Dysfunction: Dialysis, Continuous Ambulatory Peritoneal Dialysis (CAPD)

Common Clinical Manifestations: Joint Pain and/or Muscle Pain, Abnormal Fluid Retention, Third-Space Fluid

Body Characteristics: Obesity

In the form "THERAPY PROTOCOL", the doctor and the pharmacist may view the most recent treatment protocol, as well as older ones, searching them by the date of treatment (figure 4).

Figure 4: Therapy Protocol form on CarciWard. In this Form, there is a List of Drugs, the Defined Dosage and Administration Rate, the Manner of Infusion (IV Push, IV Infusion) Depending on the Injectable Chemotherapeutic Agent, the Chemotherapy Protocols, the Solvent Compatible with Each Anticancer Agent, the Approved Volume of the Infusion Solvent and the Infusion Rate of the Final Solution.

There are also three subsections, presenting current "Treatment Medicines", "Pre-Chemotherapy Medicines" and "Post-Chemotherapy Medicines". Under those

sections there are lists with drugs (listed by generic name), the defined dosage and administration rate, the manner of infusion (IV push, IV infusion) depending on the

injectable chemotherapeutic agent, the chemotherapy protocols, the solvent compatible with each anticancer agent, the approved volume of the infusion solvent and the infusion rate of the final solution. The program suggests a particular dose and administration rate for a patient, calculated automatically based on patient's BSA. The doctor may intervene and alter the dose and the administration rate, if that is considered necessary. He/she may also view lab tests by selecting the appropriate key, and modify doses or administration rate based on test results. At this stage, the program sets questions concerning patient's biochemical values. The answers the user gives add up and then it appears a final order concerning the alterations that need to take place on the treatment schema. The pharmacist is entitled to read preparation instructions and print the labels that will be stuck on the vessels carrying the solutions.

The form "ADMINISTRATOR'S INFORMATION" contains any kind of

information the administrator may need to use in order to add or alter fields and data in the software program. If for example, an outdated chemotherapy agent needs to be substituted with a new one, the administrator may store the new information in this form, in order to incorporate it in "CarciMed" later, or vice versa.

Using a Jarque-Bera hypothesis test we observed that the two datasets did not follow the normal distribution for the BSA, dosage, and time values. We therefore performed a Wilcoxon non-parametric rank test for statistical comparison between paired samples. A p value of less than 0.05 was regarded as statistically significant. Significant difference was observed in BSA values ($p=0.0391$) and dosage ($p=0.0042$) between "Carci" and doctor. However, no significant difference was observed for the time of injection ($p=0.4814$) between "Carci" and doctor.

Table 3: Median Values for BSA, Dosage and Time Compared between "Carci" and the Manual Preparation by the Doctor.

Table 3. Median Values			
Variable	CarciWard	Doctor	p-value
BSA (m ²)	1.82	1.8	0.0391
Dosage (mg)	857.33	200	0.0042
Time (min)	40	60	0.4814

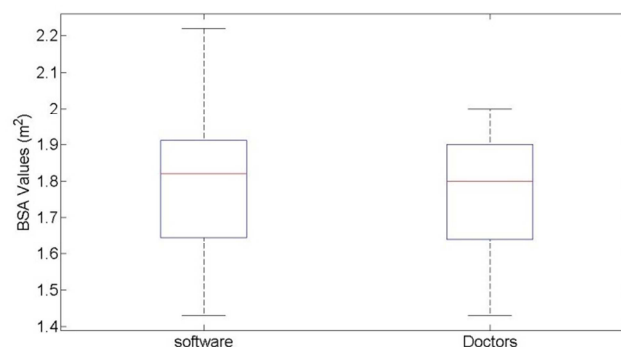


Figure 5: Boxplot of the BSA Values, Carci vs Doctors, with the Median in Red.

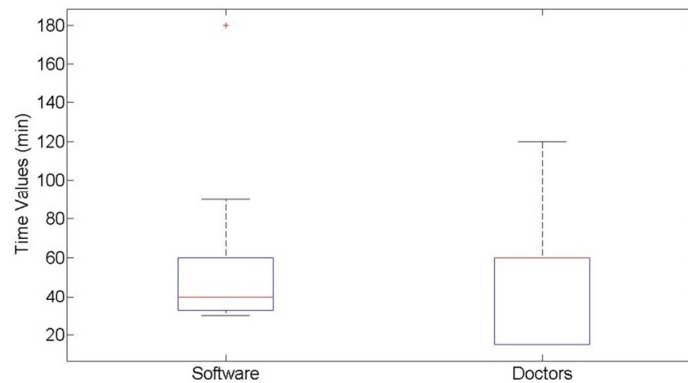


Figure 6: Boxplot of the Time Values, Carci vs Doctors, with the Median in Red.

Discussion

Excellent organizational skills, knowledge competence and professional responsibility are three major characteristics that clinical staff needs to have. All members of the clinical staff need to know what their exact duties are in order to complete their tasks fast, accurately and without being distracted from information and data that are unnecessary to them.

“Carci” has been developed to facilitate the work of hospital and clinic professionals, by providing all those data and information needed to carry out the daily work. The fact that a nurse does not have access in the same forms as the doctor prevents the first from getting confused and wasting time with unnecessary information, while it authorizes the second to grant data security and confidentiality. Work is done faster and in a more responsible manner, since each one who enters the program, has named access only. Thus, the name of the person who adds, deletes or modifies data, may be viewed at any moment by the colleagues. This means that information and decisions made on protocol selection or modification, drug doses, drug replacements and administration procedures are all name-signed.

The program also functions as a database for treatment protocols and prescribed medication. The “CarciWard” administrator, who has access to all 5 forms of the program, is entitled to add,

delete or modify protocol and medication related information, as long as new and improved agents are launched in the market. The database may be constantly updated by the system vendor and thus, doctors get informed about new anti-cancer agents and other related drugs, without making any effort to search for new products. It is virtually impossible that all doctors are aware of all anti-cancer medications that exist in the market, so a database providing this information as well as drug combinations (protocols) is really valuable for them.

The prevention of error occurrence is another advantage of the particular program. Using a manual method to calculate BSA and medication doses, there is an increased risk in error making. However, errors in dose’s measurements can be fatal. Our study was the first prospective study to demonstrate the application of CarciWard in clinic. Despite the relative small sample of patients, a significant difference ($p=0.0042$) in the calculated dosage of the chemotherapeutic agents was found between the CarciWard and that prescribed by the doctor. This reflects the need for a precise protocol that it will eliminate the possibility of an occasionally fatal event. CarciWard produces a detailed protocol for the preparation of the chemotherapy treatment, describing the procedure step by step and giving the precise amounts for each. Apart from miscalculations, errors may also occur when writing or typing the

name of a medicine. Having a database where a doctor can select a specific chemotherapeutic agent or other supportive medications reduce the possibilities for the occurrence of errors¹³⁻¹⁹.

Apart from an anti-cancer protocol and medication database, the program serves as a patients' record, where all patient-related information is stored and can be retrieved even years later, such as in cases of relapse. Paper and folder filling are not necessary, since all patient information may be stored in the program. Patient data and information can be used for statistical analysis and for research purposes, by the clinics of pharmaceutical companies.

"Carci" is designed initially for use in local facilities. In cases where a patient needs to move to a different clinic, data can be easily exported and imported within the "Carci" system. Access on patient's data through internet will be promoted once secure settings are implemented on the system given the degree of confidential data kept on the system.

Conclusion

In summary, "Carci" is a software tool that enables us to make fast and precise preparations of injectable anticancer agent mixtures. Although this has been a pilot study, "Carci" may be a promising software tool for the safe management of medication in cancer chemotherapy.

Conflicts of Interest

The authors have no conflict of interest relevant to the subject of this article.

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