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Dose intensity in standardized health technology assessment in oncology

PROJECT ASSUMPTIONS AND AIMS

Principal aim of the project is to contribute to the development and standardization of health technology assessment (HTA) methodology in the field of clinical oncology. Project is not only of theoretical importance but implies also development of practically acceptable software tools that can help in implementation of the above mentioned principles in clinical practice.

HTA methodology brings a very wide spectrum of problems and scientific challenges, the project however will be focused namely to the field of longitudinal evaluation of anti-tumour therapy and associated assessment of reached results. These aspects are still not adequately addressed even in internationally available standards and there is substantial variability among different oncological specializations. The main aim of the project is to contribute to the evaluation of complications associated with anti-tumour therapy both from prospective and retrospective point of view. Prospectively applicable criteria should improve optimization of supporting therapy and finally thus reduce probability of risk events.

The project will propose set of standard endpoints that should be associated with distinct health care episodes. It means not only categories of reached complex therapeutic response, but also evaluation of dose intensity parameters (e.g. dose reductions, dose delays, relative dose intensity of actual treatment, etc.), complications including toxicity grading and explained consequences for anti-tumour therapy. Planned software tools should bring these standards into clinical practice.

Regarding specific problems of Czech oncology, the project proposal was motivated namely by following facts:

- there is still no unified set of standard measures for longitudinal monitoring of anti-tumour therapy and running results; although some fields of oncology (e.g. pediatric oncology) already accepted this evaluation according to international protocols, widely applicable standards are not available – this fact embarrasses both retrospective and prospective health technology assessment
- nearly all installed hospital information systems have no parametric data entry for running monitoring of anti-tumour therapy, serious adverse event and in most of them, there is no space for computer-assisted planning of therapeutic plans; this situation represents serious drawback in health care quality evaluation and makes prospective optimization of supporting care impossible.
- numerous Czech clinical institutes and hospitals have recently adopted modern software information systems for orders and preparation of chemotherapy, implemented into clinical practice – these early phases of development seem to be ideal for implementation of standardized evaluation rules.
- leading Czech clinical teams reveal strong professional attitude towards implementation of therapeutic plans, not only for pharmacotherapy and RT, but also for time-related detailed dosage schemes.

Both theoretical and practical outputs of the project will be prepared in form that allows their presentation and application in international level.

Project Dose Intensity as Oncology Standard is supported by AMGEN s.r.o.

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PROJECT AIMS AND OUTCOMES

1. To prepare documentation that defines endpoints of separated health care episodes in different fields in oncology with special emphasis on often neglected aspect of dose-intensity.
2. To prepare prospectively applicable standards for therapeutic plans and their longitudinal evaluation, including reasons of plan violation. To include project documentation "Dose – intensity as endpoint in standardized anti-tumour therapy" into official methodology of Health Technology Assessment to be adopted in guidance of Czech Society for Oncology.
3. To implement routine evaluation of proposed endpoint (including dose intensity) in existing models for HTA. There will be developed an expert SW system that will be able to follow complex parametric monitoring of disease development including longitudinal evaluation of therapeutic plans accomplishment (e.g. parameter of actual total dose intensity, relative dose intensity, reasons for dose delays and dose reductions, etc.).
4. To ensure pilot service carried out by developed software tools and collection of relevant clinical data in model studies. On the basis of acquired data, to prepare model methodology for other potential users in Czech Republic or other countries.
5. Powerful scientifically oriented presentation of the results and software tools in clinical conferences and seminars held by Czech Society for Oncology and Czech Ministry of Health. To prepare all outputs with adequate project documentation and to enable their availability for clinical institutions under guarantee of Czech Society for Oncology.

PUBLICATION PLAN

All official outputs of the project will be issued both in Czech and English language (software workspace, project documentation, manuals for users, papers, web presentation).

Project is aimed to bring out project documentation as special edition in book format (published as official, reviewed material, under the auspices of Czech Oncological Society, in collaboration of involved guarantees and AMGEN company). The material will summarize theoretical principles of the project, proposed model solution and practical guidelines for implementation in different types of clinical institutions.

Second key outcome of the project will be devoted to developed software, i.e. user manual and project documentation. Publishing of these issues will make the tool widely available.

As an output of model studies gathering data from different diagnostic groups (see below – phase IV of the project) several scientific papers will be prepared. These titles can not be precisely specified at the moment, but their content will correspond to the project aims: dose intensity as an indispensable component of complex health technology assessment in oncology, model clinical studies. The papers should be targeted to the following potentially acceptable international journals: Neoplasma, Breast Disease, The Journal of Supportive Oncology, Cancer Investigation.

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Project outputs will be presented in renowned Czech and international conferences /lectures, posters/: Czech national oncology conference /Oncology days in Brno/ 2005, 2006; ECO 2006; Health Technology Assessment International Society Congress 2005.

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ACKNOWLEDGEMENTS

Development of data standards and implementation of HTA principles in oncology is supported by Ministry of Health Care of the Czech Republic. Development of DIOS portal and SW tools is supported by AMGEN company through research grant bestowed upon Czech Society for Oncology.

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DIOS

Dose intensity as oncology standard

User's manual

Project Dose Intensity as Oncology Standard is supported by AMGEN s.r.o.

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Introduction

What is DIOS?

DIOS is a web portal with software tools and information regarding chemotherapeutic treatment of oncological patients. It is mainly about chemotherapeutic regimens that are presently used, its definition and adherence in clinical practice.

Whom is DIOS for?

The DIOS Portal is focused widely and is intended for the following groups of users:

- Students of oncology or others interested in these problems
- Doctors – cancerologists
- Expert groups – sharing of information, knowledge and data

Where can I find DIOS?

DIOS is a web portal, freely accessible on the Internet with common web browser.
To enter the portal, please use the following address:

http://www.cba.muni.cz/dios

What is dose intensity?

Briefly speaking it is the level of antitumor pharmaceuticals applied during chemotherapeutic treatment. Its amount is measured in milligrams per week per square meter of body surface. This measure is important because it is related to treatment result and adverse effects level.

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Main Page

When you enter the address http://www.cba.muni.cz/dios into your web browser, you will get to the home page of DIOS portal.

The Web Portal DIOS aims to collect and offer information about chemotherapeutic regimens for all oncological diagnoses of solid tumors. Moreover, the DIOS portal offers software tools for work with chemotherapy regimens – searching for suitable regimens, calculator of applied dose intensity, sophisticated analytical tools and so on. The web portal is in English except of the database tools, national support is being prepared.

The main page offers basic information about the portal and also it is the main guidepost of the portal. Navigation is available using buttons in upper left panel. The following sections are accessible from the main page:

- Project DIOS
- Map of the portal
- Methodical guidelines

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- Educational outputs
- Results and reporting
- Software tools
- Project news

Project DIOS

Link to the portal home page. It contains basic information about the portal and its topics.

Map of the portal

This link displays detail structure of the whole portal. It offers quick orientation and navigation for users interested in overall content or quick navigation to desired part of the portal.

Methodical guidelines

Methodical guidelines bring information and links regarding the way of dose intensity assessment, methodology of calculation of single parameters, implementation of chemotherapy assessment in hospitals and more. This section has more technical character and it is intended for users with deeper interest in computation and analysis problems in dose intensity field.

This part is in preparation phase and will be finalized during the year 2006.

Educational Outputs

This part of the portal contains materials for users interested in problems regarding chemotherapy of solid tumors. Some of these materials describe in general basic principles and methods of application of contemporary chemotherapy, other describe single diagnoses or chemotherapeutic regimens. Only approved publications are presented here, verified by a specialist in given area.

This part is in preparation phase and will be finalized during the year 2006.

Results and reporting

This branch of the portal will present the outputs of studies running under the auspices of DIOS portal. Access to these data will be restricted according to their character and sensitivity.

The content of this branch of the portal will depend on acquired data. It will be filled successively starting 2006.

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Software tools

A set of tools which are designed for data collection and evaluation not only in the field of applied chemotherapy. Details of this portal section are presented further in this document.

Project news

News about the whole project DIOS are presented here. It is a valuable source of information for regular visitors of the portal DIOS.

Registered users can log in with their username and password by pressing button Login.

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Software tools

Software tools is a set of internet applications which allow collecting, evaluate and present data concerning chemotherapeutical regimens. Dose intensity evaluation is one of their main purposes.

They are divided into three categories:

- Analytical tools
- Database tools
- Patients electronic records tools

Analytical tools

The analytical tools are the basic type of on-line tools which provide dose intensity evaluation. They act on entered ad-hoc chemotherapeutic schedules or on large collections of clinical data. The analysis tools consist of the Dose intensity calculator and the Therapy organizer. The former one quickly calculates a dose intensity of an entered chemotherapeutic schedule, while the latter one may be used to design a particular chemotherapeutic schedule. Details of these tools are given further in this document.

Database tools

The database tools are designed to collect electronic data and to browse and search for useful information. Particularly the **DIOS registry** is a web-based application for gathering detailed data about applied chemotherapies and the **CORIS registry** is a web-based system for gathering parametric clinical data of oncologic patients. These database-oriented tools allow user-friendly data collection through internet without need to install any local software. Local as well as multicentre studies are supported. The collected data may be passed into the available analysis tools. Czech language support has been implemented already and the english localization is going to be ready during 2006.
The third database tool is the **Central library of chemotherapeutic regimens**. It contains definitions of schedules which are in use. Interested visitors are allowed to search by basic criteria such as a diagnosis or a disease phase. The library has been recently filled with data about chemotherapeutic regimens in breast cancer.

Patients electronic records tools

Analytical and graphical presentation of collected data about oncological patients can be performed by the Comprehensive Data Browser (COBRA) which is a functional overlay of the database system CORIS.

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This tool has been already prepared and its launch depends on the oncology data availability. It is going to be on-line during 2006.

There are four modes of user's interaction with the software tools:

- educational mode
- ad-hoc user
- registered user
- multicentric registry

Educational mode

This mode of interaction is appropriate for a user who wants to get basic knowledge about chemotherapeutic regimens and dose intensity assessment. The Central Library of CHT regimens, the Dose intensity calculator and the Therapy organizer – all these tools fall into the educational mode. The user equipped with these tools is able to try to assess the dose intensity in particular chemotherapeutic schedules.

Ad-hoc user

Chemotherapy experts - clinical oncologists are also able to use the same tools as in the educational mode. Explicit input and output data are supposed in this mode of interaction.
The available tools allow a physician to check the dose intensity level achieved by particular patient. In addition, the physician can use the Therapy organizer to design a chemotherapeutic schedule for particular patient. The entered information may be used only once. Neither saving nor batch evaluation are supported in this mode. However, the physician is allowed to print the data. Higher functionality is provided for registered users only.

Registered user

Registered users can access besides the basic analysis tools also the database tools which allow them to make up a collection of their patients. The collection may be then browsed and analyzed by the available analysis tools or the complex system COBRA.

Multicentric registry

All the described tools are available in this mode including a database system designed for multicentre data collection. The system is geographically unlimited, data are centralized and on a secured database server ensuring data protection as well as broadband access.

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Dose intensity calculator

Dose intensity calculator offers the possibility to evaluate the observance of doses of actually applied cytostatics in comparison with predefined standard.
It enables viewing and testing of the calculation of dose intensity of selected regimens in one chemotherapy cycle and also recording and saving of applied doses and evaluating of the whole chemotherapy of selected patient.

Calculator is also joined with the second tool – the therapy organizer.

For entry to the calculator press Software Tools button in the main window of the portal and then press the button with text DI calculator in displayed window. Than introductory window of calculator is opened.

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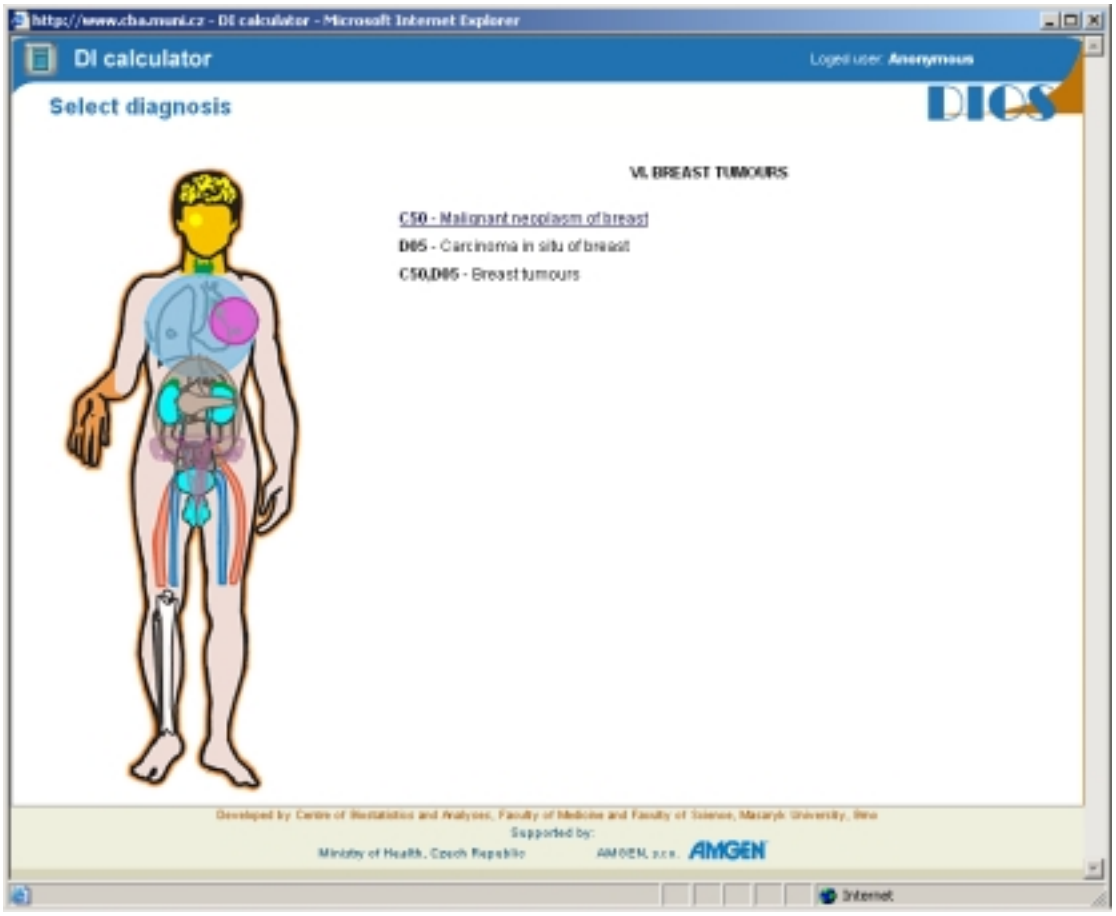
By clicking on *Continue to Select Diagnosis* window enabling the selection of oncological diagnosis is displayed. For selection of diagnosis hover cursor over human organ in displayed figure and choose from offered diagnoses.



In the pilot portal version there are available only chemotherapeutical regimens for diagnosis of the breast carcinoma C50.

After selection diagnosis the user enters to the window for selection of selected chemotherapeutical regimen that are predefined for particular diagnoses. In addition to chemotherapeutical regimen it is necessary to enter initial surface of patient's body (BSA) and patient's weight. Opening the window with detailed chemotherapy description is possible to perform by clicking Create New Therapy button.

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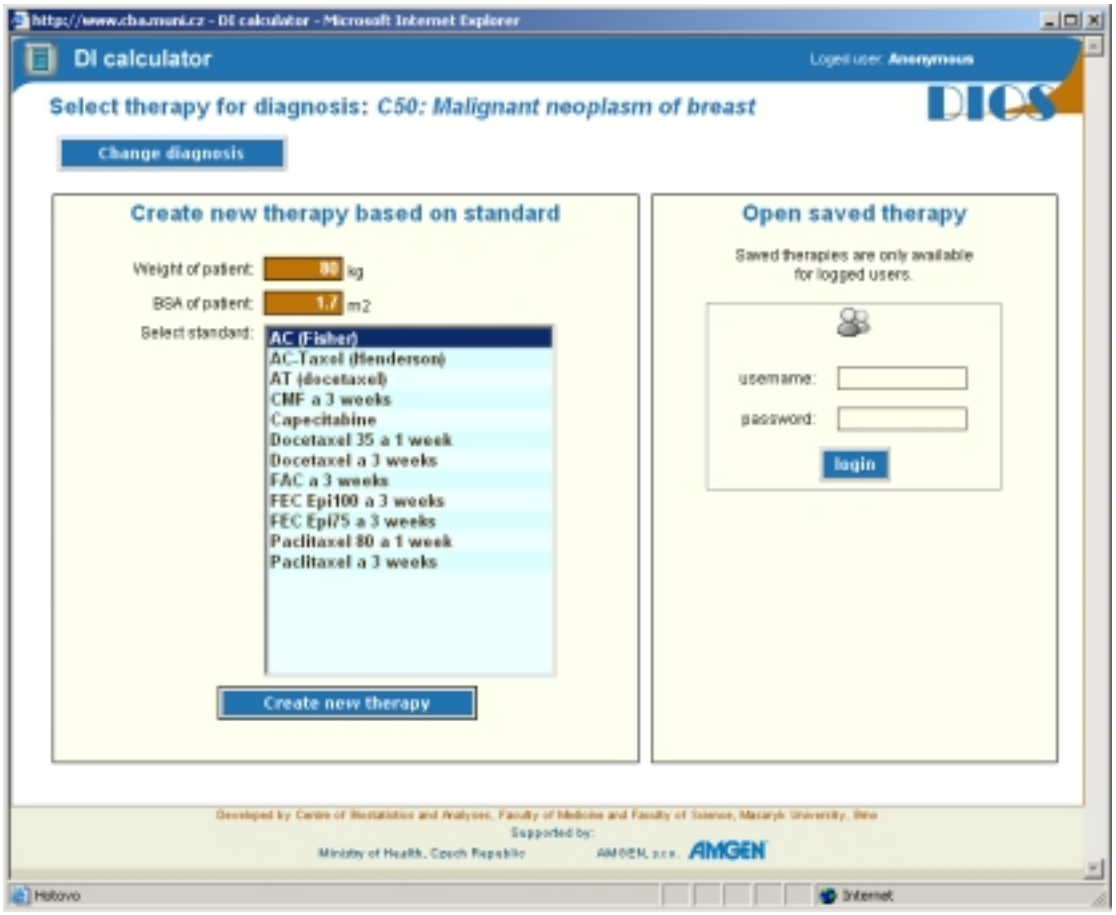

Calculator window displays calculated standard doses of cytostatics of selected chemotherapeutical regimen and enables to enter actually applied doses of cytostatics. Calculator automatically calculates achieved values of dose intensity separately for each applied cytostatic. The abbreviation of cytostatic is stated in column headline. For full title of cytostatics it is necessary to click on stated abbreviation. For easier navigation fields for user entry data are brown coloured. The user can also use help tools as graphic calendar for selection of requested data and small calculator for calculation of body surface from patient's high and weight data.

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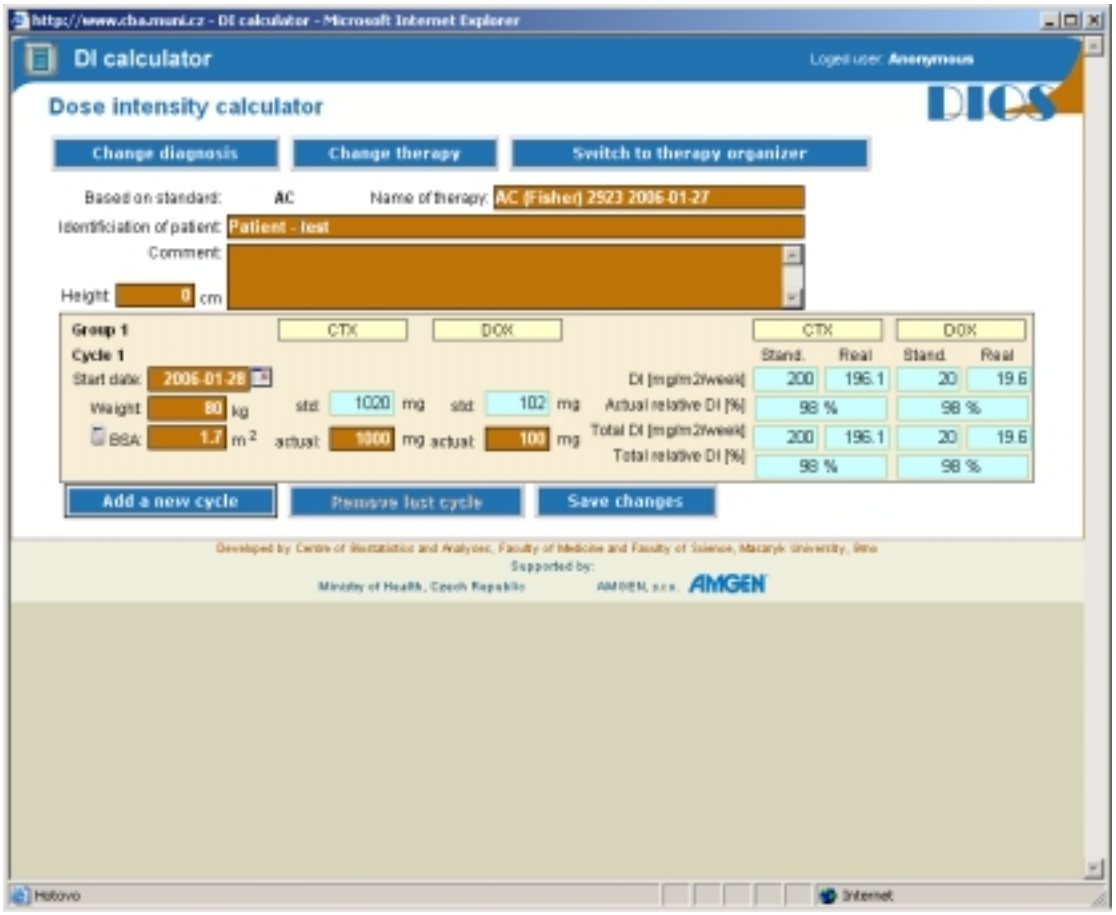
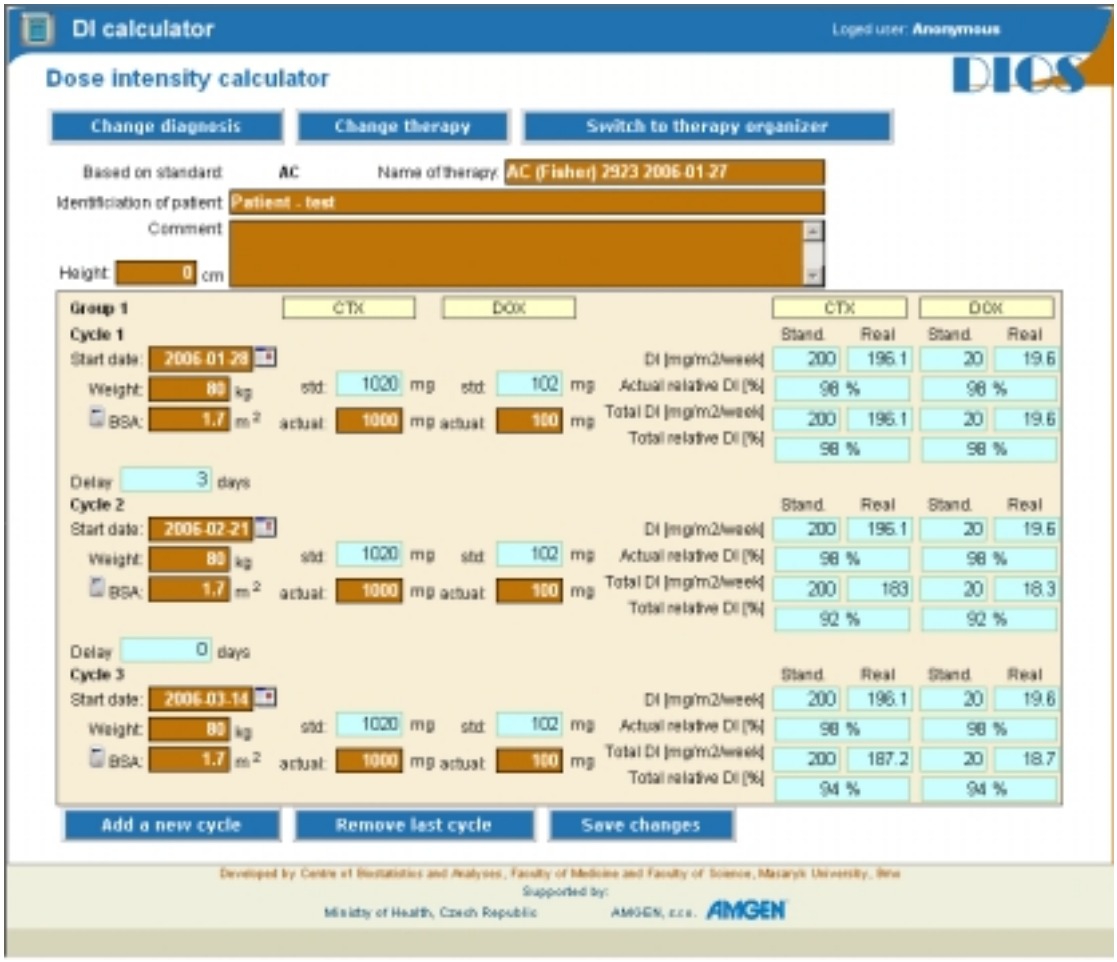


In the initial configuration of window calculator only one chemotherapy cycle is evaluated. For evaluation of other cycles of given chemotherapy it is necessary to press *Add New Cycle* button. In opened window fields for next cycle are displayed. They are prefilled with data from previous cycle. The user can only correct fields where dosage was changed. Last cycle can be removed with *Remove Last Cycle* button.



Function *Save Changes* for saving of engaged applied doses is accessible for registered users.

Calculator in the pilot version calculates for each cytostatics following parameters:

- Standard dose – dose of cytostatics recalculated for engaged body surface in one cycle
- Standard dose intensity – dose intensity of the standard regimen in one cycle
- Actual dose intensity – actually achieved dose intensity in one cycle
- Actual relative DI – rate of actually achieved and standard dose intensity in one cycle

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- Standard total DI – standard dose intensity for the whole chemotherapy

- Actual total DI – actually achieved dose intensity in the whole chemotherapy

- Total relative DI – rate of total actual and standard dose intensity

Therapy organizer

The Therapy organizer is a tool that offers the chemotherapy planning according to predefined standard chemotherapeutic regimen. The tool is able to design the time schedule for chemotherapy dosage for selected patient.

To enter the organizer press *Software Tools* button in portal window and than therapy organizer in displayed window. Opening window of planner is displayed.

By clicking on *Continue to Select Diagnosis* window enabling the selection of oncological diagnosis is displayed. For selection of diagnosis hover cursor over human organ in displayed figure and choose from offered diagnoses.

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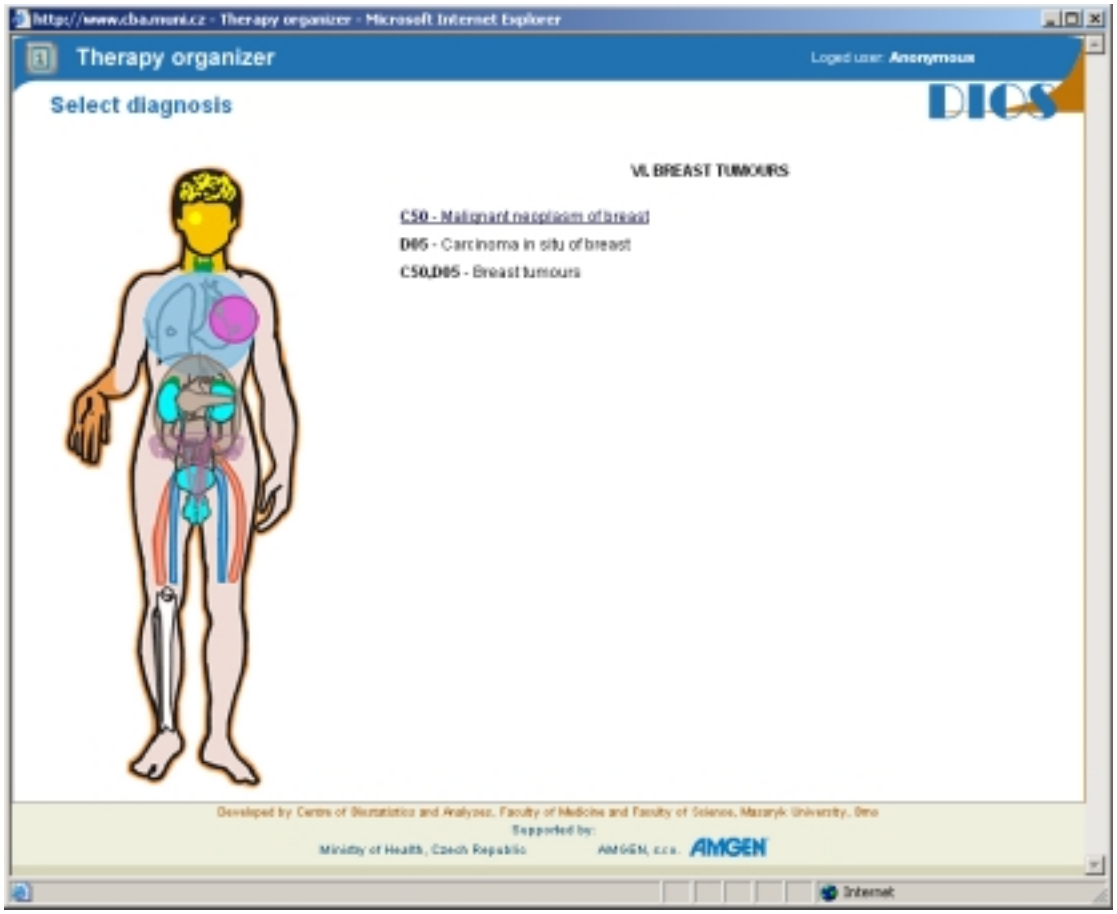

In the pilot version of the portal there are available only chemotherapeutical regimens for diagnosis of breast carcinoma C50.

After selection of diagnosis the user enters to the window for selection of selected chemotherapeutical regimen that are predefined for particular diagnoses. In addition to chemotherapeutical regimen it is necessary to enter initial surface of patient's body and patient's weight. Opening the window with detailed description of chemotherapy is possible to perform by clicking at *Create New Therapy button*.

In the planner window it is possible to enter data of start of the therapy, initial value is actual date. For projection of changes to the application schedule press *Save Changes* button.
Planned cycle calculation is possible to select by repeated press of *Add a New Cycle* button.
Resulted schedule of particular applications is displayed in the bottom part of the planner window. Prepared schedule can be printed by clicking *Print* button.

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Dose Intensity Protocols

Dose Intensity Protocols is planned as the tool that automatically evaluate data acquired from database tools (DIOS, registry, CORIS registry) and it offers summarized report primarily aimed for observance of dose intensity for selected group of patients.

Development of this tool is closely dependent on the success of above-mentioned tools and pilot collections of test clinical data. Launching of the tool is planned within the year 2006.