

## Developing inquiry skills through scaffolded use of a simulation

Cindy E. Hmelo<sup>1</sup>, Sailesh Ramakrishnan<sup>2</sup>, Roger S. Day<sup>2</sup>, William E. Shirey<sup>2</sup>, Qingshou Huang<sup>2</sup>, Joseph Baar<sup>2</sup>

<sup>1</sup>Until August 10:

Learning Research and Development Center, 816  
3939 O'Hara Street  
University of Pittsburgh  
Pittsburgh PA 15260  
email: hmelo+@pitt.edu

After August 10:

Dept of Educational Psychology  
Graduate School of Education  
10 Seminary Place  
New Brunswick NJ 08903

<sup>2</sup>University of Pittsburgh Cancer Institute

Paper or Poster Presentation

### Abstract

Teaching students the skills of planning and interpreting experiments is difficult. Students tend to focus on obtaining desired outcomes rather than on understanding causes and effects. Inquiry skills are increasingly important for students entering the health professions who may later conduct large-scale research such as clinical trials or be required to interpret the results of such research. To learn how to design and interpret the results of experiments, these students must have appropriate experiences and support to help shape the experience, model the inquiry process, and encourage reflection. Simulations offer promise for providing these experiences. One such simulation environment, the Oncology Thinking Cap (OncoTCap<sup>1</sup>) provides a comprehensive modeling workbench for cancer researchers. This tool is versatile and can be used to model clinical trials, but its functions and operation may impose excessive cognitive load for the novice. Also, novices may have little knowledge of the kinds of experimental designs used in cancer research. There are well-defined designs for clinical trials of new drugs, used at different stages of testing and for different purposes. As Baker and Dunbar (1996) note, the expert scientist often has a mental schema with slots to be filled with the items needed to determine an experimental design. Work on software-realized scaffolding suggests that communicating the design process is one way that learners can begin to construct these schemas. In this paper, we report on the design, use, and evaluation of a special purpose interface, the Phase II Trial Design wizard, to help scaffold medical students' design of an experiment to test a new cancer drug.

**Keywords:** scientific inquiry, simulation, software-realized scaffolding, problem-centered learning

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<sup>1</sup> This software is available for downloading at [http:// www.pci.upmc.edu/tcap](http://www.pci.upmc.edu/tcap).

## **Developing inquiry skills through scaffolded use of a simulation**

Teaching students the inquiry skills of planning and interpreting experiments is difficult. Students often focus on getting desired outcomes rather than on understanding the effects of their actions (Schauble, Klopfer, & Raghavan, 1991). Domain-specific inquiry skills are increasingly important for students entering the health professions who may later conduct large-scale research such as clinical trials or be required to interpret the results of such research. To learn how to design and interpret the results of experiments, learners need to have appropriate experiences and support to help shape the experience, model the inquiry process, and encourage reflection (Kolodner, 1997; Collins, Brown, & Newman, 1989). Simulations offer promise for providing abundant and inexpensive opportunities for learners to design, run, and interpret the results of experiments. Computational tools have greatly expanded the sophistication of simulations. But using these simulations may impose excessive cognitive demand. Novices may not have constructed an appropriate mental schema for designing experiments (Baker & Dunbar, 1996). We can help students learn such a schema by communicating the important slots that need to be filled as they design experiments. In addition, allowing students to simulate their experiments and observe the results provides the dynamic feedback needed to enhance their understanding of both the process of experimentation and their knowledge of the domain (Schauble et al., 1995). In this paper, we describe scaffolded use of a professional modeling tool to help medical students learn to design the clinical trial of an anticancer drug. Based on theories of software-realized scaffolding, we have designed a “wizard” to communicate the process of designing a clinical trial (Hmelo & Guzdial, 1996). This wizard helps learners set up the trial that they can then simulate using the Oncology Thinking Cap (OncoTCap), a modeling tool for simulating the behavior of heterogeneous population of cancer cells. The schema slots are highlighted through screen-based forms that allow the needed input for setting up the model in OncoTCap.

## **Clinical Trial Design**

The process of bringing a new drug to market is complex. A drug must go through several stages of laboratory and clinical testing before it can be available for general use (Simon, 1993). Phase I of clinical testing involves a small number of patients. Its aim is to identify a safe dose. A phase II trial may be subsequently conducted to see if there is any clinical response to the drug. In the design process, the researchers choose a single dosage and schedule for the drug. The researchers specify several minimal operational characteristics of the study and a design is chosen to meet those criteria. Typically, the goal is to distinguish a low response rate from a high response rate with good accuracy. A phase III trial compares a new drug against existing treatments to determine whether it is more effective. We developed software-realized scaffolding to help students learn to design Phase II clinical trials. In this study, students were guided through an iterative process of design followed by trial simulation to optimize their design.

We hypothesized that there are several aspects of trial design that are important, some of which are not salient to novices. The more obvious elements of a Phase II clinical trial design include:

- Background information about the disease being treated and the drug being tested
- Criteria for including/ excluding patients
- Considering the results of preclinical and phase I testing
- Specifying the dosage, treatment schedule, and treatment duration

Some of the schema elements that should be less obvious to the students are:

- Conditional rules such as modifying the drug dosage as a result of toxic side effects
- Conditions under which the patient will stop receiving the experimental protocols
- Operational characteristics needed for determining how many patients will be included in the study, and of that group, how many responses need to be observed to conclude that the drug is worthy of further study.

We have implemented the Phase II Clinical Trial Wizard on the foundation of OncoTCap.

### **OncoTCap**

The Oncology Thinking Cap is a computer-based modeling laboratory for conducting experiments in cancer biology. The core concept underlying OncoTCap is that tumors are composed of heterogeneous

populations of cells and this forms the basis for understanding cancer (Fuji et al., 1996). OncoTCap can model the important concepts in cancer research and treatment such as cell cycle control; cell growth, death, and repair mechanisms; mutational processes, treatment characteristics, resistance, and schedules; and genetic characteristics (Day et al., 1998). OncoTCap models these processes by specifying the different properties of cancer cells such as their genetic make-up, location, and resistance (Ramakrishnan, et al., 1998).

To form the foundation for the Trial Wizard, OncoTCap has to model a basic description of the target domain of breast cancer. Using OncoTCap, we described a model that included parameters for cell cycling time and turnover of the cell population, drug resistance pathways such as Multi Drug Resistance, bypassing certain genes, and abnormal genetic pathways due to mutations. The model includes a tumor location description with the breast being the primary location and possible spread to the liver and lung. OncoTCap also includes a description of the hypothetical drug, Pittamycin together with the means to represent a regimen of drug applications and simulate their effect on tumor growth. With an initial cell count, a description of the cell heterogeneity, and a definition of the drug Pittamycin, OncoTCap performs a Monte Carlo simulation of breast cancer (Day et al., 1998). In this simulation, tumor cells grow based on their cell kinetics parameters and the nature of their heterogeneous properties. The schedule and applications of the drug reduce counts of different tumor cells based on dose and drug definition.

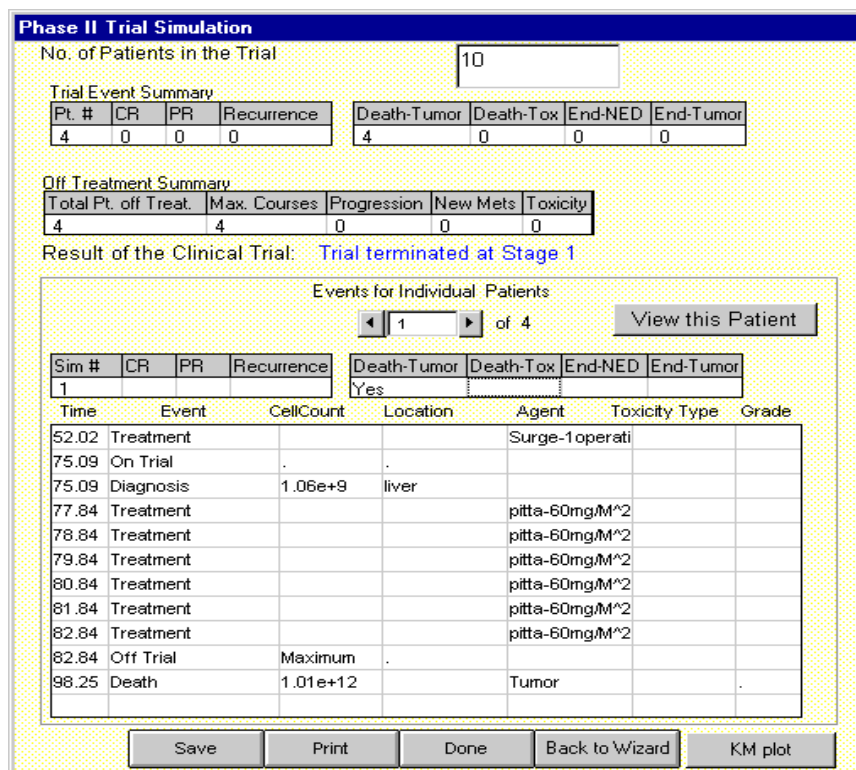
OncoTCap provides two different ways of displaying the Monte Carlo simulation. In the Cancer Patient Simulator, the interactive simulation of tumor cell growth is shown by means of a graph of the number and characteristics of tumor cells in a single patient. The relative cell counts of the various different cell types determined by the heterogeneous properties are shown in different colors. The event window shows different clinical and simulation events such as simulation start, diagnosis, tumor spread, treatment, and death.

The Multiple Patient Simulator (MPS) runs the same Monte Carlo simulation as the Cancer Patient Simulator over many patients. Its display does not show interactive graphs. While the simulation is running, the MPS window shows a tally of the number of patients simulated, the number of responses, cures, and deaths. At the end of the simulation, the MPS window also displays the event lists for each patient. A modified version of the MPS is used in the Trial Wizard (See Figure 1).

### **Phase II Clinical Trial Wizard**

A *Wizard* in a computer program is a set of simple screens that walk the user through a complex cognitive task. The task is differentiated into multiple subtasks, reducing the cognitive load required to complete the task. The task in this case was the design of a Phase II trial for study of the efficacy of the drug Pittamycin in the treatment of Metastatic Breast Cancer (i.e., breast cancer that has spread to other organs). Scaffolding using a wizard provides support to the user in two ways. First, the user is made aware of the expected components in a Phase II Clinical Trial by the contents of the various screens. Second, the user can accomplish the task by concentrating on one subtask at a time with less effort and confusion than if approaching the task as a whole. The screens of the wizard allow the user to easily navigate from one subtask to another and back again as needed.

The computer supported clinical trial design and interpretation process can be divided into 4 components. The first component is the Introduction screen, which describes the objective of the wizard and the information the user will need to provide in the rest of the screens. The second component consists of a set of 4 well-defined steps that lead the user through the subtasks. In these screens, the user can input the various design parameters for the trial such as the Schedule (Figure 2), Dose Modifications due to toxicity (Figure 3), Off treatment criteria (Figure 4), and Statistical Criteria (Figure 5). The third component is the Summary, where the user's trial design from steps 1- 4 are summarized in natural language and the user can click a button to run this simulation in the Multiple Patient Simulator (Figure 1). The modified MPS, which actually runs and displays the results of the clinical trial, forms the fourth component of the process. There is easy navigation between the various screens in the wizard via



**Figure 1: Modified Multiple Patient Simulator summarizes the results of the simulation and allows students to examine individual patient event histories**

“next” and “back” buttons. The MPS has a “back to the wizard” button, which enables the user to view the results of the current trial and go back to the wizard to make further modifications to the design and re-run the trial. The final summary screen also provides the user with the ability to print out the description of the trial design. The MPS allows the user to print out the results of any simulation run.

## Methods

We tested the Phase II wizard with 24 fourth year medical students who were divided into 6 groups of 4 students each. Each group of students worked cooperatively at a computer for a 2-hour session. Prior to the session, they were asked to develop a research proposal for a Phase II trial of the fictitious drug, Pittamycin. Students were given preclinical information and the results of a Phase I trial. This information included the maximum dose that was tolerated by patients (MTD) and the types of toxicities that were observed (neurological function and blood formation). The students first used the wizard to design and simulate the Phase II trial they had designed before coming to the lab. The first

author facilitated the group's work by 1) asking students to summarize their initial proposal, 2) helping them with the any interface problems they might have had and making sure that they understood relevant software features, 3) asking them to justify their changes, and 4) encouraging them to reflect on what they learned from this experience.

Each run of the wizard generated a printout of the groups' design. In addition, students printed out the results of the simulation that represented their group's final design.

We assessed individual and group learning using data from five sources: 1) classroom observations, 2) printouts of design summaries for each simulation run 3) group clinical concept sheets pre- and post-software 4) individual critiques of a flawed concept sheet, and 5) a questionnaire that asked about various aspects the software. The design summaries contained all the characteristics the students specified: the dosage and schedule, any conditional rules for dose modification and removing patients from treatment, and the statistical considerations.

The goal of this exercise was for students to create clinical concept sheets. Clinical concept sheets are research proposals for testing a new drug. The students received a one page instruction sheet that briefly specified what should be included (i.e., introduction and background, significance, methods, risks and benefits). Students worked on this task in groups. The groups completed their first concept sheet before using the software and a second draft post-simulation. To assess individual learning, we asked students to critique a flawed concept sheet. This was a proposal for a fictitious drug that was active against lung cancer. The concept sheet was 1.5 pages, including instructions. The students were asked to list any problems that they found and for each, explain why it was important. The critiquing task was completed 3 times: before the students produced the first draft of their concept sheet, after they wrote the first draft, and again after the simulation. This within-subject design allows us to see what was learned from designing a study without and then with scaffolding.

**Phase II Clinical Trial Wizard - Step 1: Schedule**

Treatment Schedule : Please enter  
 (1) your patient's treatment schedule (i.e., Week 1 [Days 1, 2 and 3], Week 2 [Days 4 and 5], etc...) by clicking in the appropriate boxes,  
 (2) the drug dose, and  
 (3) the frequency with which you want the cycle repeated.

pittamycin

Week 1	Week 2	Week 3	Week 4
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Dose :  mg/M<sup>2</sup> per day

Repeat this course after :  Days

When you have completed these tasks, click Next

Cancel < Back Next > Finish

Figure 2: Step 1 of the Clinical Trial Design Wizard: Defining the dose and schedule

**Phase II Clinical Trial Wizard - Step 2: Dose Modification due to Toxicity**

Dose Modification Due to Toxicity.

If your patient experiences a particular grade of drug toxicity (0=none, 4=severe) at a selected site, you may assign mandatory dose-reduction criteria to prevent irreversible drug toxicity.

By clicking on the appropriate selection, you may decide whether the dose reduction applies to the next treatment, or the rest of the treatment. When you have completed these tasks, click Next.

if Toxicity is  and grade >= , then reduce dose by  %

for Next Treatment  for Rest of the Course  for All Remaining Courses

if Toxicity is  and grade >= , then reduce dose by  %

for Next Treatment  for Rest of the Course  for All Remaining Courses

Cancel < Back Next > Finish

Figure 3: Step 2 of the Clinical Trial Design Wizard: Modifying the dose due occurrence of toxicity

**Phase II Clinical Trial Wizard - Step 3: Off Treatment Criteria**

Off-Treatment Criteria.

Select the circumstances under which your patient will stop receiving drug treatment by checking the appropriate boxes and assigning numerical values when needed.

When you have completed these tasks, click Next.

If the  th course has been completed

If the primary tumor increases by  % over baseline

If NEW metastases appear

If toxicity grade is >=

Cancel < Back Next > Finish

Figure 4: Step 3 of the Clinical Trial Design Wizard: Deciding when individual patients will be taken off-treatment

**Phase II Clinical Trial Wizard - Step 4: Trial Design**

Trial Design. Assign the statistical parameters for the design of your clinical trial. On the basis of this information, the Wizard will determine (1) the optimal patient sample size and (2) the minimal number of patients that must respond to treatment in order to conclude that the drug is active. When you have completed these tasks, click Next.

Probability of accepting poor drug (alpha) :

Probability of rejecting good drug (beta) :

Response probability of poor drug :

Response probability of good drug :

**Calculate Optimal Trial Design**

First Stage Sample Size ( n1 ) : 4 Stop and reject drug if # responses < or = ( r1 ) : 0

Total Sample Size ( n ) : 11 Reject drug if total # responses < or = ( r ) : 2

Cancel < Back Next > Finish

Figure 5: Step 4 of the Clinical Trial Design Wizard: Setting the statistical parameters

## Results and Discussion

**Using the simulation.** The six student groups ran an average of 8.67 simulations during their sessions. The student's first simulation run was an implementation of their initial proposal. For the majority of the groups, their initial dosage and drug schedule was consistent with the MTD identified in the Phase I trial information they received. In the first run through the trial wizard, when students reached the screen where they could set conditional rules for dose modification, students in all the groups expressed surprise. In their pre-computer

session concept sheet, students wrote about monitoring patients for toxicity, but they did not specify the actions to be taken if toxicities were observed. The students did not initially add these rules and remained consistent with their original design. They were less surprised when they had to consider the off-treatment criteria. Although poorly specified in their initial designs, the students understood the importance of setting these criteria. Finally, students specified the operational statistical characteristics of the clinical trial design. The program then computed the number of patients needed and the number of responses that would allow them to conclude that the drug had some clinical activity and was worthy of further study. The facilitator tried to elicit student understanding of these statistical considerations, but this remained a murky area for the students. Following this, students simulated running the trial they had designed. The MPS summary included information about patient responses, deaths due to tumor, and deaths due to drug toxicity. The students closely watched the cumulating results. They were able to view a survival plot that allowed them to see the increase in median survival time. This helped the students appreciate the therapeutic effect of the treatment. Their other concern was that along with any responses they observed, there were often many patients that died due to drug toxicity. Their perusal of individual patient records, particularly in the first few runs, led students to a deeper understanding of (1) the types of toxicity that occurred, (2) how long they took to resolve, and (3) why responses tended to occur fairly early in the treatment process.

This concern with toxicity led all groups to add dose modification rules in their second design. This screen was an important focus for student discussion about the nature of different types of toxicity. For example, students noted that neurologic toxicity caused very severe consequences (i.e., death of brain tissue) and only resolved slowly, whereas toxicity that impaired the body's ability to make new blood cells resolved quickly and was treatable. Thus, students tended to be conservative about dose modification for brain toxicity and would severely reduce the dose; they were more liberal in tolerating blood cell toxicity.

Although students discussed the importance of only changing one variable at a time in order to understand the results of their experiments, this is rarely what they actually did. On the first few runs,

the students changed 2-3 variables per run but this decreased over time. This may have occurred partly because the students were trying to manage multiple goals: maximizing responses while minimizing deaths due to toxicity. A strategy that several groups converged on involved using a very large dose of the drug early in the treatment and allowing time for the body systems to recover from the toxicity before giving another dose of the drug. This was effective because it killed tumor cells before they developed resistance to the drug. The students were clearly engaged in the iterative design and simulation process. When asked to reflect on what they had learned, students often mentioned statistics and an appreciation for the complexity of designing a clinical trial.

**Student assessment and evaluation of software.** The pre and post concept sheets were coded for the 24 elements of the Phase II clinical design schema; the concept sheet critiques were graded similarly for the 20 elements that were missing from the concept sheets. In the post-computer session concept sheets, all groups modified their initial design to include specific dose modification rules and stop-treatment rules. They also specified their statistical parameters more completely. This suggests that students were constructing more elaborate trial design schemas. This elaboration is consistent with the scaffolding provided by the wizard. The conditional rules (dose modification and off-treatment criteria) and statistical characteristics were either not fully specified or not considered in the initial trial designs but were included after students were made aware of these factors in the wizard. The pre- and post- concept sheets were coded for the components needed for a complete trial design. The mean score for the initial trial design was 14.83 out of a possible 24 points ( $SD=4.07$ ). The students improved on their post-research proposals to a mean of 19.83 ( $SD=1.55$ ;  $t(5)=2.89$ ,  $p<0.05$ ).

Students became better at critiquing the flawed clinical concept sheets. There were 20 components missing from the concept sheet used in the assessment. The mean number of missing components identified by students was 3.60 ( $SD=2.28$ ) before the initial trial design, 4.67 ( $SD=3.25$ ) after the initial design, and 6.92 ( $SD=2.60$ ) after the computer session. There was a significant improvement as a result of the computer session ( $F(1,23) = 8.77$ ,  $p<.01$ ). This effect was largely a result of improved knowledge of how to plan the treatment (including conditional rules for modifying dosages

and taking patients off-treatment). Because the students spent much of their time engaged in adjusting the treatment plan, this is where we expected to see the greatest effect.

The students rated the wizard positively, with a mean of 4.07 out of 5 on questions that asked students about different aspects of the learning environments' ease of use, helpfulness for learning, and understandability. They ranked this activity second only to their clinic time in value (students also received lectures and participated in a journal club). Their comments indicated that they liked receiving the rapid feedback on their experiments and having the opportunity to change variables and rerun their study.

### **Conclusion**

Constructivist approaches to teaching and learning stress the importance of teaching scientific inquiry in the context of authentic problems that integrate both the inquiry process and subject matter learning (Collins, Brown, & Newman, 1989; Schauble et al., 1995). Working on authentic tasks, however can be extremely difficult for novices and requires additional support. This study demonstrates the effectiveness of scaffolding students' scientific inquiry using a professional modeling tool. Using the clinical trial wizard, we help the students learn about the various components of the clinical trial design process. The dynamic feedback combined with ease of iteration proved crucial in allowing students to optimize their trial designs. Students went from a rudimentary Phase II trial schema to one that was much more elaborated after working with the OncoTCap trial wizard. Our observations suggest that students used these tools not only to focus on the inquiry process but to discuss important issues in cancer treatment as well.

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