MEDINFO 2021: One World, One Health – Global Partnership for Digital Innovation
P. Otero et al. (Eds.)

doi:10.3233/SHTI220190

Expanding Access to CNS-TAP: Design, Development, and Initial Use of a Complex Precision Health Specialty Web App for Neuro-Oncology

Karthik Ravi[a,b], George Meng[a], Holly J. Roberts[b], Allison Schepers[c], Andrea Franson[b], Carl Koschmann[b], Bernard L. Marini[c], Allen Flynn[a]

[a] *Department of Learning Health Sciences, Medical School, University of Michigan, Ann Arbor, MI, USA,*
[b] *Department of Pediatrics, University of Michigan Medical School, Ann Arbor, MI, USA*
[c] *University of Michigan College of Pharmacy, Ann Arbor, MI, USA*

Abstract

This paper offers a case study to demonstrate how a complex scoring model tool called CNS-TAP, originally created by a neuro-oncology team at one institution, was upgraded and made accessible to a wider audience. In the Results and Discussion, many issues of web app design, development, and sustainability are covered. Overall, we chart a path to expand access to many unique software tools created and needed by today's medical specialists.

Keywords:

Drug Therapy, Medical Oncology, Clinical Decision Support Systems

Introduction

A longstanding medical informatics challenge is to provide the necessary software application support for medical specialties and subspecialties. While electronic medical records (EMRs) are evolving, they still only support common clinical workflows and not the unique workflows of many specialists. To fill in this gap, prior efforts in informatics, like SMART apps [1] and CDS Hooks [2], have enabled EMRs to be extended to meet more information needs and better support specialists' workflows. Meanwhile, in everyday practice, specialists rely on a host of other software tools outside of EMRs.

As custom forms, spreadsheets, and other similar information tools created by specialists become more extensive, useful, and well-known, requests are made to share and expand the use of these "homegrown" and proprietary tools. Scaling-up access and expanding the use of specialist-made tools is a significant informatics area of need. This paper details how one complex homegrown spreadsheet tool was redesigned and reimplemented as a precision neuro-oncology web application that can still be controlled and managed by its small team of expert specialist originators.

CNS-TAP Application Context

In the subspeciality of pediatric neuro-oncology, diagnoses of brain tumors are devastating and generally confer a dismal prognosis. In practice today, promising targeted drug therapies to treat brain cancer may inadvertently be overlooked due to an inability to incorporate individual tumor biology and other factors that allow medications to be selected systematically with molecular precision [3].

Our team members originally used spreadsheet software to create the first Central Nervous System Targeted Agent Prediction Tool (CNS-TAP) [4]. CNS-TAP formalizes a utility model to evaluate, score, and rank more than 50 drug agents used to treat brain tumors in children. This "scoring model" in CNS-TAP combines pharmacokinetic, genetic, and blood-brain barrier permeability information with expert consensus-based scoring of published evidence of drug effects. Overall, CNS-TAP's scoring model has nine criteria, 6 of which are intrinsic to drugs (e.g., quality of in vivo data) and 3 of which are patient-specific (e.g., the proportion of tumor that has the targetable genetic alteration). The tool scores and ranks agents relevant to individual patient cases using its complex evidence-based scoring model. For specialist users in neuro-oncology, CNS-TAP makes it easier to generate consistent, comprehensive, individualized drug treatment recommendations (Fig. 1). CNS-TAP also lays important groundwork for routine, evidence-based precision medication selection in other areas of oncology.

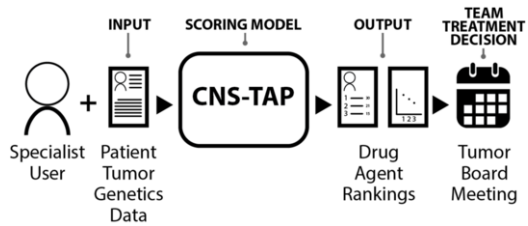

Figure 1 – General CNS-TAP application workflow

Prior to the current project, the CNS-TAP spreadsheet tool was used only locally to generate patient-specific drug rankings periodically. As a spreadsheet, the CNS-TAP tool is cumbersome to use for report generation. The spreadsheet format also hinders extensive sharing of CNS-TAP's scoring model with external users since the model requires ongoing updating and tight version control. To address these limitations and bring CNS-TAP to an expanded audience of pediatric neuro-oncologists nationwide, we designed, developed, and have started using a new implementation of the CNS-TAP scoring model built into a widely accessible web application.

Here, we present our design methods, development work, and sustainability plans for the new CNS-TAP web app. We hope sharing this material will stimulate more development of accessible tools for medical specialists.

Research Questions

To meet our objective of expanding access to CNS-TAP, we asked and answered the following research questions related to its design and development as a web app.

RQ-1: What core capabilities are needed by practicing neuro-oncologists to make the CNS-TAP app suitable and functional for informing precision medication selection?

RQ-2: What design challenges pertain specifically to reimplementing the original CNS-TAP spreadsheet tool as a web app, and how can they be overcome?

RQ-3: What design opportunities pertain specifically to reimplementing the original CNS-TAP spreadsheet tool as a web app, and how can they be realized?

RQ-4: What *ongoing web app management tasks* must be attended to for the CNS-TAP web app to be sustainable?

Methods

To realize a widely accessible CNS-TAP web app, we first aimed to understand the app's requirements and core capabilities. We began by analyzing the use of the original CNS-TAP spreadsheet and by doing the other user-focused research outlined below.

First, we witnessed and documented how the current CNS-TAP spreadsheet is used to generate drug ranking reports for specific patients. Next, we developed four detailed personas describing anticipated CNS-TAP users acting in the roles of medical specialists, cancer researchers, app administrators, and app content managers. We elicited and responded to feedback on these four personas from the pediatric neuro-oncology lab and clinical team that originally developed CNS-TAP at Michigan.

With an understanding of the workflow and the personas in mind, next, we produced an App Design Document using Adobe Illustrator. For some user interface elements, e.g., an array of toggle buttons, we intentionally gathered design solutions from other websites, mobile apps, and relevant app and visual design materials [5]. Ultimately, our App Design Document listed user sensibilities (e.g., seriousness and professionalism) and included fonts, a color palette, and a series of wireframes for potential interactive onscreen user views. We again returned to our neuro-oncology colleagues to review and improve the designs in the App Design Document. This process led us to prioritize building an app with a simple landing page followed by a single-page web application with a few functional elements that can be easily turned on or off.

Using the App Design Document as a guide, we created a minimum viable web app product (MVP) with the low-code Knack platform (knack.com). Several versions of this MVP were shown to our neuro-oncology colleagues and other stakeholders to gather feedback on design elements, usability, and core functionality. Subsequent changes in the App Design Document were made. In the end, we arrived at a complete prototype MVP version of CNS-TAP by accounting for almost all of the feedback coming from our design meetings with specialists.

Then, using the MVP as a guide, we undertook custom web app development. The current CNS-TAP web app online (cnstap.org) was built primarily by authors KR and GM using agile methods and pairing. We followed good documentation and software development practices. The app is built in JavaScript using Vue. It uses two APIs to ingest CNS-TAP's evolving scoring model information. These APIs were enabled by the ongoing open-source Knowledge Grid effort for computable knowledge management at the University of Michigan (kgrid.org).

During the four months of custom CNS-TAP web app software development, several design challenges arose due to the limitations of modern browsers, Vue, and JavaScript (e.g., onscreen design of graphs for displaying drug agents and their scores). In these cases, we again made wireframes constrained by what was technically possible. When then returned to our neuro-oncology users to gain their preferences and advice on design changes.

Throughout the CNS-TAP web app development process, we kept notes and drafted technical and end-user documentation. We were especially careful to note and document the work needed to continue to maintain, manage, and run the CNS-TAP as a web app after its development and deployment for wider access and use.

Results

To address RQ-1, we created this list of core capabilities for a minimally functional CNS-TAP web app:

1. A target biochemical pathway selection feature where the user can toggle on and off buttons for each target pathway in the tool (Fig. 2 - Top)
2. An editable table that is linked to the pathway selection feature and contains intrinsic drug values and patient-specific columns for all drugs in the tool (Fig. 2 - Top)
3. An appropriate and easily interpretable graph visualization of the baseline and patient-specific CNS-TAP scores for the relevant drug agents (Fig. 2 – Bottom Left)
4. A one-click automated custom PDF report generator capable of producing a report encompassing CNS-TAP's outputs
5. Space where the user can enter custom annotations, reminders, and case commentary to support future tumor board presentations

Regarding RQ-2, next, we list and discuss the following design challenges that we faced during the design and development of the CNS-TAP web app.

1. The need to include numerous ($n \approx 20$) target biochemical pathways as user-selectable options
2. The need to embed and fully explain CNS-TAP's complex scoring model inside the newly developed web app
3. The need to indicate that input of patient-specific information is optional for scoring drug agents using the CNS-TAP scoring model
4. The need to design an easily interpretable graph visualization of the baseline and patient-specific CNS-TAP scores for all drug agents within user-selected target biochemical pathways

To resolve challenge #1, we decided to use togglable buttons, which act as filters of the drug table. That way, the user can easily and quickly toggle target pathways of interest on and off in a dynamic fashion (Fig. 2 - Top).

To resolve challenge #2, we included a custom informational dialog box linked to a button entitled 'Scoring Criteria,' which explains all nine criteria CNS-TAP uses along with other scoring model details (Fig. 2 -Top).

With regards to challenge #3, patient-specific information spans six columns of the drug table in the app (three input columns and three columns with corresponding scores). Hence, we decided to make these six columns hidden at first and viewable via a button when a user wants to input patient-specific values (Fig. 2 - Top). This makes it more obvious that a user can also use the CNS-TAP app without any patient-specific inputs.

For challenge #4, adding a graph visualization posed the largest design challenge and comprised a critical aspect of our discussions with app stakeholders. The initial graph visualization used in reports created with the spreadsheet tool displayed a two-pronged double-axis where one axis arranged the patient-specific drug agent scores and the other arranged the corresponding baseline scores. For the app, our design decisions for a new graph visualization came about through multiple iterations of different possible ideas. Since simplicity was a driving force in our design for these graphs, we favored a single graph rather than two (Fig. 2 – Bottom Left). Color-coding and shading were added to distinguish between baseline and patient-specific CNS-TAP scores in the web app graphs.

Regarding RQ-3, here we share some web app *design opportunities* that go beyond what spreadsheet software can do and that emerged during our work to enhance the usability and functionality of the CNS-TAP web app.

1. Use of a table that easily expands and collapses
2. Use of informational Tool Tips
3. Automatic generation of custom PDF reports
4. Embedded support for new CNS-TAP users
5. Addition of a Disclaimer, End User License Agreement (EULA), and Single Sign-on

Opportunities #1 and #2 were employed to decrease the cognitive burden placed on the user by simplifying the interface and reducing the busyness of the user's view.

The rows for drug agents in the table expand and collapse immediately as the user toggles target biochemical pathways on and off. This way, users can quickly generate lists of all drug agents related to one or more specific target biochemical pathways of interest.

The three patient-specific columns used in the CNS-TAP web app can also be easily shown or hidden at the click of an obvious on-off button.

To help users throughout their sessions of app use, the new web app has Tool Tips that appear upon hovering with a mouse pointer and show a variety of information, such as scoring weights, hyperlinks to relevant scientific papers, and descriptions of the scoring model factors.

For Opportunity #3, seeing that clinicians need to present the outputs from CNS-TAP at Tumor Board meetings and in other settings, the app was enhanced to generate PDF reports automatically containing the app's outputs. The PDF reports include the drug table with the selected pathways, the graph of the CNS-TAP scores, and any notes entered by the specialist user during their session.

For Opportunity #4, we took into consideration the needs of new CNS-TAP users. For new users, we recognized that navigating the large drug table and having numerous togglable buttons may be confusing. To address this, we added a built-in, on-demand tutorial (Fig. 2 – Bottom Right). This tutorial efficiently walks new users through a series of nine logically arranged steps, eventually showing them every core feature and how that feature works. In addition, we created and linked to an instructional video that exhibits a typical CNS-TAP user workflow for a single patient. Finally, we created a detailed user manual that provides written instructions on how to use the CNS-TAP tool and explains its features.

For Opportunity #5, working in conjunction with the Office of Technology Transfer at the University of Michigan, we are taking critical legal, security, and privacy precautions with the CNS-TAP web app. A Disclaimer has been added, and we are currently working on adding an End User License Agreement and Single Sign-on capabilities using Okta (okta.com). We found that web apps enable certain legal, security, and privacy protections in ways that spreadsheets do not.

Regarding RQ-4, we have created the following list of items that need to be attended to by the team of neuro-oncology specialists supporting the CNS-TAP web app for the app to be kept up-to-date and for end-user access to the web app to be sustained over the long term.

1. Additions to the number of drugs included in the app and corresponding advancement of drug agent scoring model
2. Software code base management
3. Routine deployment of app upgrades
4. Management of Single Sign-On capabilities

For Item #1, the team is planning to continue to review and update the scientific evidence base of the app (i.e., the drug agents and their features) on a quarterly basis.

In addition, the team routinely performs a thorough literature search to retrieve the latest research information on the target biochemical pathways and drugs in the app.

Regarding item #2, we continue to use Github to store and manage the CNS-TAP app's codebase and the computable evidence base for the scoring model. At quarterly meetings, enhancements to the scoring model are decided on by the neuro-oncology experts on the team. These changes are documented at these meetings and then applied to create the next version of the CNS-TAP app.

For Item #3, currently, app deployment is done using Heroku. App releases in Github are directly pushed to Heroku, allowing for a reliable technical app update process.

For Item #4, work is near completion to add appropriate legal and security precautions into the web app. We are also adding a straightforward user registration and authentication workflow using Okta to leverage user accounts in common online systems (e.g., Google Drive). This Single Sign-on capability does require some active configuration and management by the CNS-TAP team.

Discussion

By combining effective web app design and development practices with innovative approaches to computable knowledge management, we upgraded a locally-used specialist software tool to be accessible via the World Wide Web. This change in the app's accessibility has made CNS-TAP easily accessible for

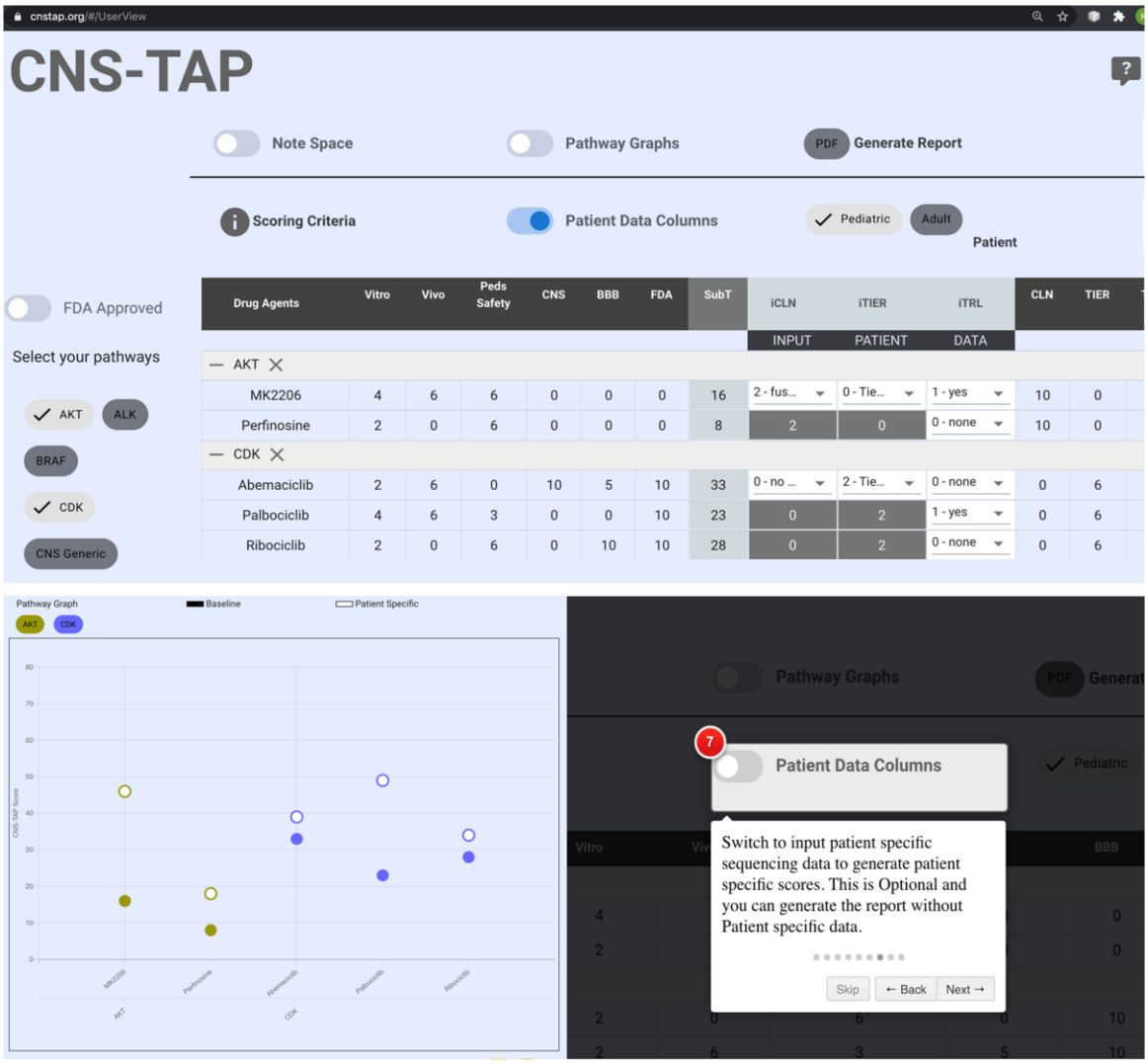

Figure 2 – Top: CNS-TAP's drug scoring and ranking table. Bottom Left: A graph view showing drugs and scores. Bottom Right: A snapshot of the in-built tutorial function inside the CNS-TAP web app

the first time to a national audience of neuro-oncology experts in two organizations, the Pacific Pediatric Neuro-Oncology Consortium (PNOC) and the Children's Brain Tumor Network (CBTN).

CNS-TAP's drug scoring model represents a novel effort in the field of pediatric neuro-oncology to create and apply an evidence-based scoring algorithm to systematize how precision drug selection with patient genetic information unfolds when treating brain tumors. Since January 2021, the new app has been used to support an ongoing clinical trial within PNOC. Plans for further collaboration with the CBTN are also being developed.

Although the CNS-TAP tool is currently used mostly for cases of high-grade pediatric gliomas, the scoring model and existing web app architecture remain extensible. With some additional effort, the scope of the scoring model and the corresponding CNS-TAP app can be extended to cover additional target biochemical pathways for other types of brain tumors. Discussions are underway to expand the target pathways to cover medulloblastomas.

This project reveals the importance of taking an interdisciplinary approach to building web applications for clinical specialists. The clinicians, pharmacists, and software developers on the CNS-TAP team all made crucial contributions to the new CNS-TAP web app.

This project also highlights a widely applicable design lesson. It remains vital to establish a detailed understanding of specialist user workflows. In this case, we saw that specialists using CNS-TAP put the outputs from the tool into presentations for Tumor Board meetings. We made this presentation-building process more efficient by enabling the new CNS-TAP web app to generate meeting-ready PDF reports automatically.

We learned notable lessons about the sustainability of web apps. Since CNS-TAP's scoring model requires regular enhancement, thoughtful knowledge management of the app's evidence base is key. For this reason, along with end-user docu-

mentation, we have created scoring model management and upkeep documentation for the scoring model APIs used by the CNS-TAP app as well.

The next steps for this project include the development and testing of a "batch client app" for clinical researchers. This app will apply versions of the same numeric scoring model used by the CNS-TAP web app to process tabular data about many patients in one go for research.

In this paper, we have contributed an informatics case study in transforming a locally-used homegrown tool created by and for medical specialists at one institution into a much more widely accessible software tool that can be accessed and used by other specialists at many institutions. Our case study exemplifies many informatics lessons. In particular, it illuminates the collaboration and teamwork involved in making the transformation from a locally used tool to a widely accessible one. As similar projects to increase accessibility to specialists' tools arise, we hope that the 12-month process we went through to go from spreadsheet to web app can be accelerated significantly via more advanced informatics approaches.

Finally, what is most important to patients is that – with this new support for the uptake of precision drug selection during nationwide clinical trials of childhood brain cancer treatments – learning can result about the value of precision medicine in tackling this horrible disease.

Conclusions

Through this project, we converted the specialist CNS-TAP tool from its original spreadsheet form to a more accessible web app form. By so doing, we have opened CNS-TAP and its precision drug selection model to a wider national audience. This move has also stimulated a new dialog about CNS-TAP's scoring model and prompted more collaboration between neuro-oncologists and other clinicians working in pediatric neuro-oncology. The work to design, develop, deploy, and sustain specialist web apps like the CNS-TAP web app remains considerable. Making this work more efficient is a critical target for better informatics solutions.

Acknowledgements

We are greatly appreciative of the funding received from the ChadTough Foundation and Chad Carr Pediatric Brain Tumor Center that made this software design and development project possible.

References

[1] J.C. Mandel, D.A. Kreda, K.D. Mandl, I.S. Kohane, and R.B. Ramoni, SMART on FHIR: a standards-based, interoperable apps platform for electronic health records. *Journal of the American Medical Informatics Association*, **23** (2016), 899-908.

[2] CDS-HOOKS. https://cds-hooks.org/ Accessed: May 13, 2021

[3] M. M. Li, M. Datto, E.J. Duncavage, S. Kulkarni, N.I. Lindeman et al. Standards and guidelines for the interpretation and reporting of sequence variants in cancer: a joint consensus recommendation of the Association for molecular pathology. *Journal of Molecular Diagnostics* **19** (2017), 4–23.

[4] J.R. Linzey, B.L. Marini, A. Pasternak, C. Smith, Z. Miklja, L. Zhao, C. Kumar-Sinha, A. Paul, N. Harris, P.L. Robertson, and L.M. Hoffman. Development of the CNS TAP tool for the selection of precision medicine therapies in neuro-oncology. *Journal of neuro-oncology*. **137** (2018), 155-169.

[5] E. Tufte. The visual display of quantitative information (1983).

Address for correspondence

Contact the first author, Mr. Karthik Ravi, at ukarthik@umich.edu.