ORIGINAL PAPER

Free Educational Android Mobile Application for Radiobiology. Evaluation of Radiation Oncologist and Medical Physicist

Camil Ciprian MIRESTEAN^{1,2}, Alexandru Dumitru ZARA^{3,4}, Roxana Irina IANCU^{4,5},
Dragos Petru Teodor IANCU^{4,6}

Abstract

The use of mobile devices and applications dedicated to different medical fields has improved the quality and facilitated medical care, especially in the last 10 years. The number of applications running on the software platforms of smart phones or other smart devices is constantly growing. Radiotherapy also benefits from applications (apps) for TNM staging of cancers, for target volume delineation and toxicity management but also from radiobiological apps for calculating equivalent dose schemes for different dose fractionation regimens. In the context of the increasingly frequent use of altered fractionation schemes, the use of radiobiological models and calculations based on the linear quadratic model (LQ) becomes a necessity. We aim to evaluate free radiobiology apps for the Android software platform. Given the global educational deficit, the lack of experts and the concordance between radiobiology education and the need to use basic clinical notions of modern radiotherapy, the existence of free apps for the Android platform running on older generation processors can transform even an old smart device in a powerful „radiobiology station.” Apps for radiobiology can help the radiation oncologist and medical physicist with responsibilities in radiotherapy treatment planning in the context of accelerated adoption of hypo-fractionation regimens and calculation of the effect of treatment gaps, a topic of interest in the COVID-19 pandemic context. Radiobiology apps can also partially fill the educational gap in radiobiology by arousing the interest of young radiation oncologists to deepen the growing universe of fundamental and clinical radiobiology.

Keywords: radiobiology, education, medical physicist, radiation oncology, smart device, apps.

Rezumat

Utilizarea dispozitivelor mobile inteligente „smart” și a aplicațiilor dedicate diferitelor domenii medicale a îmbunătățit calitatea și a facilitat îngrijirea medicală, în special în ultimii 10 ani. Numărul de aplicații care rulează pe platformele software ale telefoanelor sau ale altor dispozitive inteligente este în continuă creștere. Radioterapia beneficiază, de asemenea, de aplicații pentru stadializarea TNM a cancerelor, pentru delimitarea volumului țintă și gestionarea toxicității, dar și de aplicații dedicate radiobiologiei pentru calcularea schemelor echivalente ale dozelor de iradiere pentru diferite regimuri de fracționare. În contextul utilizării tot mai frecvente a schemelor de fracționare modificate, utilizarea modelelor radiobiologice și a calculelor bazate pe modelul liniar pătratic (LQ) devine o necesitate. Ne propunem să evaluăm aplicațiile radiobiologice gratuite pentru platforma software Android. Având în vedere deficitul educațional global, lipsa de experți și concordanța dintre educația în radiobiologie și necesitatea utilizării noțiunilor

¹University of Medicine and Pharmacy of Craiova, Craiova, Romania

²CFR Clinical Hospital, Iasi, Romania

³„Alexandru Ioan Cuza” University, Iasi

⁴„Gr. T. Popa” University of Medicine and Pharmacy, Iasi, Romania

⁵„Sf. Spiridon” Emergency Hospital, Iași, Romania

⁶Regional Institute of Oncology, Iasi, Romania

Corresponding author:

Roxana Irina IANCU, Department of Oral Pathology, „Gr. T. Popa” University of Medicine and Pharmacy, 16th Universitatii Street, 700115, Iasi, Romania

E-mail: roxana.iancu@umfiiasi.ro

de bază în practica clinică a radioterapiei moderne, existența aplicațiilor gratuite pentru platforma Android care rulează pe procesoare de generație mai veche poate transforma chiar și un dispozitiv inteligent cu performanțe limitate într-o „stație radiobiologică” puternică. Aplicațiile pentru radiobiologie pot ajuta clinicianul și fizicianul medical cu responsabilități în planificarea tratamentului de radioterapie în contextul adoptării accelerate a regimurilor de hipofracționare și a calculului efectului intreruperilor în tratament, un subiect de interes în contextul pandemiei COVID-19. Aplicațiile de radiobiologie pot, de asemenea, să umple parțial golul educațional din radiobiologie, trezind interesul tinerilor radioterapeuți de a aprofunda universul în expansiune al radiobiologiei fundamentale și clinice.

Cuvinte cheie: radiobiologie, educație, fizician medical, radioterapie, dispozitiv inteligent „smart”, aplicații.

INTRODUCTION

The use of mobile devices and applications dedicated to various medical fields has improved the quality and facilitated medical care, especially in the last 10 years, transforming many aspects of clinical medicine and facilitating the work of health professionals. The number of applications running on the software platforms of mobile phones or other smart devices is constantly growing, among the advantages of these apps being the help in clinical decisions and patient management but also the improvement of medical education in the field of radiation oncology. Radiotherapy benefits from both „all in one” applications and applications dedicated to different purposes (dose calculation, clinical staging, target volume delineation, toxicity management). The role of radiobiology in clinical practice has increased with the implementation of modern irradiation techniques that offer the possibility of delivering different doses of fractional radiation on different volumes or sub-volumes during the same irradiation session. Thus, it becomes necessary to calculate biologically equivalent doses (BED) or equivalent dose in 2Gy (EQD2) to correctly estimate the possibility of obtaining tumor control but also to predict the risk of toxicity. The need to reduce the time spent by patients in radiotherapy departments is a topical issue in the context created by the pandemic generated by the new coronavirus. Thus, the use of hypo-fractionation schemes has experienced an accelerated implementation in the new context. The use of the linear quadratic model (LQ) underlies the calculation of BED and EQD2 in different clinical scenarios but currently new data on tumor radio-sensitivity and normal tissues make it possible to create more complex radiobiological models. Radiobiology is also the backbone of fundamental research with applications in the new trials proposed in clinical radiotherapy, especially if a new fractionation scheme is considered.

The development of apps that include complex radiobiological models is proving increasingly necessary with technological development. Most apps for radiobiology are based on equations derived from the quadratic linear model that estimates biological effective dose (BED) and the iso-effect equation for estimating the tumoricid and toxic effect of fractionation schemes relative to standard fractionation^{1,2}(Equation 1,2).

BED and EQD₂ formulas:

$BED = n \times d(1 + d/\alpha/\beta)$ (Equation 1)

$EQD_2 = D \times ([d + (\alpha/\beta)]/[2 + (\alpha/\beta)])$ (Equation 2)

EQD₂ is the dose delivered in 2Gy fractions that is biologically equivalent to a total dose.

D = total dose given in Gy

n= number of treatment fractions

d = dose per fraction in Gy

α/β = dose at which the linear and quadratic components of cell kill are equal

The purpose of the study is to identify and present free apps for the Android platform dedicated to radiobiology. All applications were evaluated by a radiation oncologist with experience between 3 and 5 years using 3 smart phones with specifications: OS: Android 7.1.1 (Nougat); Qualcomm MSM8909v2 Snapdragon 212 chipset (28 nm); CPU: Quad-core 1.3 GHz Cortex-A7, OS: Android 5.0.2 (Lollipop); Chipset Exynos 7420 Octa (14 nm); CPU: Octa-core (4x2.1 GHz Cortex-A57 & 4x1.5 GHz Cortex-A53) and OS: Android 9.0 (Pie); Chipset Kirin 710F (12 nm); CPU: Octa-core (4x2.2 GHz Cortex-A73 & 4x1.7 GHz Cortex-A53) and by a medical physicist with 5 to 10 year experience in radiation oncology treatment planning, using a device with the specifications: Exynos820 - Quad-core processor (2x2.15 GHz Kryo & 2x1.6 GHz Kryo) - G9350, and a 5.5-inch Super AMOLED display.

RESULTS

Radiation oncologist evaluation:

RadioModels is a complex application that includes mathematical models applied in radiation oncology. Even if it is not an application dedicated only to radiobiology, this app should be mentioned for the complexity and advanced possibilities offered. The application provides not only prognostic and predictive models of toxicity in breast, esophageal, extrahepatic cholangiocarcinoma and bile duct cancers, head and neck cancers, pancreatic cancer, rectal cancer and thyroid cancer, including the benefit of adding radiotherapy, as well as and complex radiobiological models based on the equations of LQ, NTCP and TCP based on the Lyman Kutcher Burman (LKB) model, gaps correction factors in radiation treatment, but also the isodose-based morbidity and mortality assessment. The application also includes a module for assessing the carcinogenic risk induced by irradiation.

RBApp is a free application designed for both Android and iOS that automatically calculates BED and EQD2. Also the application allows the choice of different α / β ratios. Through the accessibility and ease with which it calculates these values, the application can be useful at the entry level medical student, radiobiologist, medical physicist, in training radiation oncologist.

BED calc is an app that calculates BED and EQD2, also providing a table with the most used values of α / β ratios. The calculation algorithm is based on the LQ model. Also, the application can be useful for the entry level for scientific purposes and for guiding the clinical decision.

RT Tools offers the possibility to calculate EQD2 and BED based on the LQ model, but also of NTCP using the mathematical formalism of the LKB model. Remarkable is the dose correction calculator for radiotherapy treatment gaps. The application offers not only radiobiology options but also scores to estimate recurrence and prognosis in breast cancer, respectively brain metastases and nomograms and risk groups for prostate cancer. RT Tools provides a Bayesian estimator for the probability of malignancy in solitary lung nodules. The application offers both educational and clinical decision support options for the entry level but also advanced notions useful to a researcher in radiation oncology or radiobiology.

LQ calc is an application that offers the possibility to calculate BED and EQD2, offering the possibility to

sum 3 therapeutic sequences with different dose fractions as well as the possibility to choose custom values of α / β ratio, with an incremental step of 0.5Gy or entered manually.

The application provides a good tool for estimating a cumulative BED or EQD2 especially for cases where two or three different fractionation schemes have been used.

Rad OncCalc offers the same possibilities to calculate BED and EQD2 but simultaneously calculates these parameters for 5 values of α / β ratio. What is worth noting is the inclusion of the recommended dose-volume constraints volume dose constraints in 3D conformal radiotherapy (3D-CRT), using mainly the recommendations Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC).

Medical physicist evaluation:

Screen display malfunctions have been found in Rad OncCalc and RT Tools. While RBApp, Rad OncCalc and Bed calculator are simple calculation modules, LQ calc can add up to 3 different dose series. The most interesting is the RT Tools application. It has a complex radiobiology module: calculation of EQD2, BED, OTT and NTCP (including organ doses). If you do not want to use a specific (paid) radiobiology app, any of these applications facilitates the work of the medical physicist and can be used to calculate equivalent doses.

DISCUSSIONS

Regarding the role of radiobiology in the current context of clinical radiotherapy, the need to know the basics of clinical radiobiology is obvious. Regarding the need for in-depth education in radiobiology and cancer biology as an essential condition in the formation of a future clinician, there are controversies. Rosenstein et al. considers that a „better” clinical radiation oncologist needs to be able to understand in depth the current knowledge of radiobiology, supporting the need to increase the number of hours of teaching radiobiology from 30 hours to 60 hours. Other experts including Robert Lee believe that an increase in the number of hours of training in radiation biology and a deepening of new notions in continuous expansion in volume and difficulty will not impact the quality of health care. Obviously, a deepening of these growing notions as a volume of scientific data will positively impact a possible research career for a radiation oncologist. As noted by the Joint Working

Group of the American Society for Radiation Oncology (ASTRO) in relation to the teaching of radiobiology, there is a worldwide decrease in the number of experts training in training radiation oncologists in radiobiology. The coverage of the need for education in clinical radiobiology is approximately 60%, with the existence in most cases of a single expert in this field in each university clinic, the number of hours allocated to teaching radiobiology ranging from 10 to > 50³⁻⁵.

Concerns in the development of computer applications that include an easy calculation of the results of the equations incorporated in the radiobiological models began with more than 10 years ago. Normal tissue complication probability (NTCP) and tumor control probability (TCP) can provide a more accurate estimation of the possibility for tumor control and the toxicity risk associated with irradiation evaluation, the equations being based on the Lyman-Kutcher-Burman (LKB) model. Parameters such as the α/β ratio, TD50 (v) defined as the tolerance dose for 50% toxicity risk for uniform irradiation of a sub-volume v of the respective organ and σ , the standard deviation of the dose = $m \cdot \text{TD50 (v)}$ (where m is the variation coefficient) are included in this radiobiological model making it difficult to calculate TCP and NTCP values. In this context, computer applications such as CalcNTCP and DORES (Dose Response Evaluation Software) developed in Visual Basic are just a few examples that have proven their usefulness and have been the basis for the development of interest in designing applications for smart-mobile phones and other smart devices in recent years⁶⁻⁹.

Analyzing software applications of interest for radiation oncology dedicated to a smart device or a mobile device a comprehensive critical review was performed by Calero et al. which identified 31 apps dedicated to iOS and Android systems. The analysis includes payable applications, the authors mentioning different objectives for which these apps were designed (from multifunctional to clinic and dose calculations). After a careful analysis, the authors recommend 3 applications

(RadOnc, Easy Oncology and iOncology) „all in one”, one in each of the 3 languages (English, German and Spanish), mentioning as a utility clinical staging, treatment-decision and dose calculators¹⁰.

CONCLUSIONS

Given the global educational deficit, the lack of experts in clinical radiobiology and the lack of concordance between education in radiobiology and the need to use basic clinical notions practice of modern radiotherapy, it is necessary to develop free apps for smart devices running on older generations processors. Existing free radiology applications now available for Android can turn even a low-cost smart device into a powerful „radiobiology station”. Apps for radiobiology can help the radiation oncologist and medical physicist in the context of accelerated adoption of hypo-fractionation regimens and calculation of the effect of gaps treatment often needed in the context of the COVID-19 pandemic. Radiobiology apps can also partially fill the educational gap in radiobiology by opening the interest of young radiation oncologists and entry-level medical physicists to deepen the ever-expanding universe of fundamental and clinical radiobiology. It is worth noting, however, the lack of complex free applications dedicated exclusively to radiobiology that include both the possibility of calculating dose compensations for treatment gaps and TCP and NTCP models and even other radiobiological models specific to a certain end point of radiation induced toxicity.

Compliance with ethics requirements: The authors declare no conflict of interest regarding this article. The authors declare that all the procedures and experiments of this study respect the ethical standards in the Helsinki Declaration of 1975, as revised in 2008(5), as well as the national law. Informed consent was obtained from all the patients included in the study.

References

1. Sharp M, O'Sullivan D. Mobile Medical Apps and mHealthDevices: A Framework to Build Medical Apps and mHealthDevices in an Ethical Manner to Promote Safer Use - A Literature Review. *Stud Health Technol Inform*. 2017;235:363-367.
2. Calero JJ, Oton LF, Oton CA. Apps for Radiation Oncology. A Comprehensive Review. *Transl Oncol*. 2017;10(1):108-114. doi:10.1016/j.tranon.2016.08.008
3. Lee WR. Radiation Biology for Radiation OncologyResidents: An Alternative View. *PractRadiatOncol*. 2019 Nov;9(6):504-505. doi: 10.1016/j.prro.2019.08.003.
4. Rosenstein BS. Teaching Radiation and Cancer Biology to Radiation OncologyResidents: A 40-Year Perspective. *PractRadiat Oncol*. 2019 Nov;9(6):392-394. doi: 10.1016/j.prro.2019.08.004.
5. Zeman EM, Dynlacht JR, Rosenstein BS, Dewhirst MW; ASTRO Joint Working Group on Radiobiology Teaching. Toward a national consensus: teaching radiobiology to radiation oncology residents. *Int J RadiatOncolBiol Phys*. 2002 Nov 1;54(3):861-72. doi: 10.1016/s0360-3016(02)02968-1.
6. Marks LB, Yorke ED, Jackson A, et al. Use of normal tissue complication probabilitymodels in the clinic. *Int J Radiat OncolBiol Phys*. 2010;76(3 Suppl):S10-S19. doi:10.1016/j.ijrobp.2009.07.1754
7. Y. Dong,B. Egleston,R.A. Price Jr.,B.S. Rosenstein, J.E. Meyer. The History of the Lyman-Kutcher-Burman Model and Its Application to the Alpha-Beta Ratio ModelingUsing Modern Statistics. VOLUME 99, ISSUE 2, SUPPLEMENT , E122, OCTOBER 01, 2017; DOI:https://doi.org/10.1016/j.ijrobp.2017.06.888
8. Khan HA. CalcNTCP: a simple tool for computation of normal tissue complication probability (NTCP) associated with cancer radiotherapy. *Int J RadiatBiol*. 2007 Oct;83(10):717-20. doi: 10.1080/09553000701570220.
9. Baumann M, Petersen C. TCP and NTCP: a basic introduction. *Rays*. 2005 Apr-Jun;30(2):99-104.
10. Calero JJ, Oton LF, Oton CA. Apps for Radiation Oncology. A Comprehensive Review. *Transl Oncol*. 2017;10(1):108-114