Radiotherapy and Oncology 109 (2013) 159–164

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Learning methods in radiation oncology

# 'Rapid Learning health care in oncology' – An approach towards decision support systems enabling customised radiotherapy' ☆,☆☆

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ARTICLE INFO

*Article history:*
Received 27 May 2013
Received in revised form 30 June 2013
Accepted 16 July 2013
Available online 28 August 2013

*Keywords:*
Radiotherapy
Decision support system (DSS)
Rapid Learning
Cancer
Tailored radiation treatment

ABSTRACT

*Purpose:* An overview of the Rapid Learning methodology, its results, and the potential impact on radiotherapy.

*Material and results:* Rapid Learning methodology is divided into four phases. In the data phase, diverse data are collected about past patients, treatments used, and outcomes. Innovative information technologies that support semantic interoperability enable distributed learning and data sharing without additional burden on health care professionals and without the need for data to leave the hospital. In the knowledge phase, prediction models are developed for new data and treatment outcomes by applying machine learning methods to data. In the application phase, this knowledge is applied in clinical practice via novel decision support systems or via extensions of existing models such as Tumour Control Probability models. In the evaluation phase, the predictability of treatment outcomes allows the new knowledge to be evaluated by comparing predicted and actual outcomes.

*Conclusion:* Personalised or tailored cancer therapy ensures not only that patients receive an optimal treatment, but also that the right resources are being used for the right patients. Rapid Learning approaches combined with evidence based medicine are expected to improve the predictability of outcome and radiotherapy is the ideal field to study the value of Rapid Learning. The next step will be to include patient preferences in the decision making.



Tailored cancer therapies, in which specific information about patients and tumours is taken into account during treatment decisions, are an important step forward from current population-based therapy [1] However, given the developments outlined below, it is becoming increasingly difficult to identify the best treatment for an individual cancer patient:

- Tumours and patients seem to be even less homogeneous than previously assumed, meaning the same treatments can have different outcomes in patients who have the same type of tumour. For instance, there are at least four molecular subtypes of breast cancer, each with very different outcomes [2]. Based on gene signatures various subgroups of tumours can be identified [3–8].
- The number of treatment options is increasing. For example, early stage prostate cancer can now be treated with conservative treatment, prostatectomy, external radiotherapy, stereotactic radiotherapy, LDR or HDR brachytherapy, high-intensity focused ultrasound, hormone therapy, combination therapies and so on. A different example is the recent rise of targeted therapies that are rapidly growing in numbers. Performing classic randomised trials to compare all new treatment options with the "gold standard" is becoming impossible by the current speed of innovation.
- The evidence for the right choice in an individual patient is inadequate. First, 'evidence-based medicine' and the ensuing guidelines always lag somewhat behind practice, particularly in highly technological, innovative and rapidly evolving fields such as radiotherapy. In addition, translating the results of clinical trials to the general patient population and environment is

☆ Data presented during the ESTRO Lecture in Geneva (ICTR meeting 2012).



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http://dx.doi.org/10.1016/j.radonc.2013.07.007

not straightforward, given the higher quality of care in clinical trials and the known selection bias (trials reach no more than 3% of cancer patients, in radiotherapy this figure is even lower) [9–11]. Finally, given the developments mentioned above – more treatment options and less homogeneous patient groups – the urgency to scaffold our treatment decisions with robust knowledge and the demand for evidence-based medicine is larger than ever.

- It is becoming more difficult to find the right evidence. Despite – or perhaps due to – the fact that papers are being published in rapidly increasing numbers (*e.g.*, as a radiation-oncologist specialising in lung cancer, has to read around eight articles per day to keep up with the literature [12]), it is difficult to match the characteristics of the individual patient to evidence from the literature and to evaluate the quality of that evidence.

The developments illustrated above have given rise to a search for an alternative to the elaborate consensus- and evidence-based guideline medicine format when it comes to making treatment decisions. The alternative discussed in this article is rapid learning [13]. Although it is known under various names, including Knowledge-driven Healthcare, Computer Assisted Theragnostics and Learning Intelligence Network, the basic idea in all cases is the (re)-use of historical data from routine clinical practice for decisions concerning new patients or to test new hypothesis [14–19] (Fig. 1). This has a number of obvious advantages, such as the large number of readily available patients and less selection bias compared to clinical trials. However, it also has some important disadvantages; for example, the quality of the data in clinical practice is much lower than in clinical trials [20]. There is a long very successful history of putting genomic data public and reusing them [3–8].

This paper provides an overview of the methods used in Rapid Learning, the initial results, and an outlook as to how the techniques involved may influence clinical radiotherapy.

## Methods and results

Rapid Learning involves four phases (Fig. 2) [13] which are continually iterated. In the data phase, data on past patients are collected, including their delivered treatments and outcomes. In the knowledge phase, knowledge is generated from these data. In the application phase, this knowledge is applied to clinical practice. In the final evaluation phase, the outcomes are evaluated, after which the first phase starts again. In every phase, external knowledge (*e.g.,* from clinical trials) is used to optimise the phase. The sections below describe the methods used and examples of typical results for every phase.

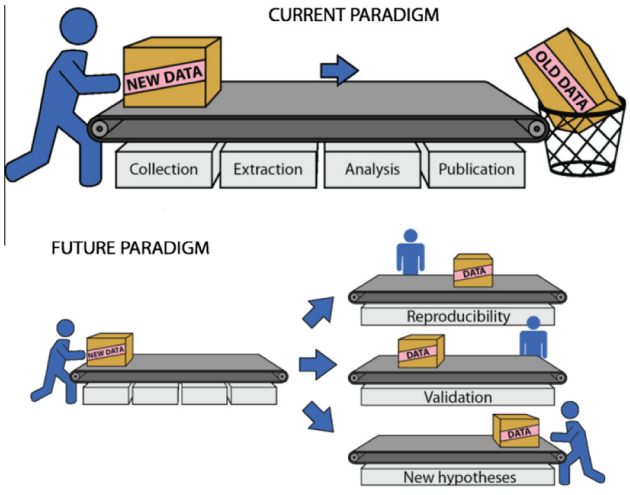


**Fig. 1.** Current paradigm versus future paradigm (modified from [43]).

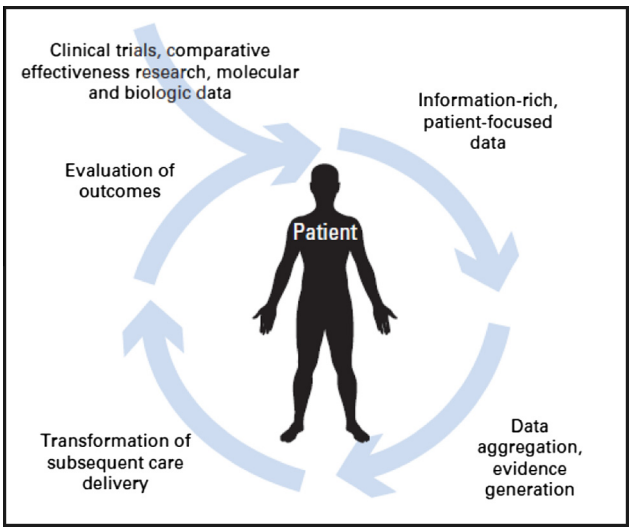


**Fig. 2.** Four phases of Rapid Learning [13].

### *Data*

Rapid Learning requires both a great deal of data and a large diversity of data. The amount of data is important (a) to obtain higher quality knowledge (the quality of the knowledge correlates with the number of patients on which that knowledge is based) and (b) to be able to generate knowledge concerning smaller, more homogeneous patient groups and/or use more variables in the knowledge phase. The diversity of the data (particularly with respect to the treatments used, but also in terms of patient characteristics) is important to ultimately decide which treatment is best for an individual patient.

Obtaining enough data of sufficient quality and diversity is the biggest challenge in Rapid Learning. This is only possible if data are shared across institutional and national borders, both academic and community health care systems. Such data sharing is hampered by a lack of time; differences in language and culture as well as data recording practices; the academic and political value of data; risks to reputation; privacy and legal aspects and so on. Nonetheless, one project that has made successful use of data sharing is euroCAT (www.eurocat.info), a collaborative project involving radiotherapy institutes in the Netherlands, Germany and Belgium. A crucial factor in the success of this project was the use of innovative information technologies, which made it possible to learn from each other's data without the data having to leave the institution (a concept known as distributed learning). Another important factor was the development of a dataset with semantic interoperability (also known as 'data with linguistic unity' or 'machine-readable data'), in which local terms are converted into concepts from a well-defined ontology (*e.g.*, NCI Thesaurus, SNOMED). In such an approach, the ontology terms serve as a common interface to the data at each institutional site, enabling a common approach to information retrieval and reasoning facilitated through a semantic portal to the data. This semantic interoperability approach also allows one to add data from clinical trials to further strengthen the data available to Rapid Learning.

The data collected in routine clinical care are often of lower quality compared to data from clinical trials. Data captured in routine care are often incorrect, contradictory, missing and biased.