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Radiotherapy for benign disorders: current use in clinical practice

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Abstract. – OBJECTIVE: The aim of this paper is to provide an update about the current clinical indications of RT in this poorly explored field outside the traditional oncological setting.

MATERIALS AND METHODS: We performed a literature search on the main databases, including PubMed, Scopus and Cochrane from their inception until 31st December 2020. An additional manual check of scientific meeting proceedings and books was conducted in order to identify all the potentially useful sources. Only essays published in English have been considered for the purposes of this analysis. The searched items included: "Radiotherapy or Radiation Therapy" and "Benign disorder or Benign disease".

RESULTS: We provided a list of current clinical indications for benign disorders based on the latest international surveys available, including major sites: eye, bone, head and neck, skin, brain, heart and peripheral vascular system.

CONCLUSIONS: Radiotherapy for benign diseases is still a feasible therapeutic strategy, which may allow to treat several invalidating conditions, especially after medical therapies have failed thus avoiding potentially invalidating major surgical procedures. A careful evaluation in selecting the indication is essential and all the choices should be thoroughly discussed with the patients.

Key Words:
Radiotherapy, Radiation therapy, Interventional radiotherapy, Benign disorder, Benign disease.

Introduction

Clinical studies reporting about radiotherapy (RT), as alternative therapeutic strategy to surgery or medical treatment in the management of several benign conditions, include a total number of almost 40.000 patients. The kind of diseases included range from hyperproliferative, to inflammatory to other functional diseases.

A few systematic reviews exist on the different topics, however, a comprehensive historical analysis published in 2003 has allowed to list more than 100 benign conditions that were successfully treated with RT.

The aim of this paper is to provide an update about the current clinical indications of RT in this poorly explored field outside the traditional oncological setting.

Materials and Methods

We performed a literature search on the main databases, including PubMed, Scopus and Cochrane from their inception until 31st December 2020. An additional manual check of scientific meeting proceedings and books was conducted in order to identify all the potentially useful sources. Only essays published in English have been considered for the purposes of this analysis.

The searched items included: "Radiotherapy or Radiation Therapy" and "Benign disorder or Benign disease".

In order to increase search reliability, considering the huge number of patients potentially includable, we focused on two different strategies:

1. Only multicenter studies, national or international surveys were accepted, single center series, case reports and other anecdotal experiences were excluded.
2. The search was focused mainly considering the latest two decades to describe. Such choice was

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made in order to account for the real current use in clinical practice and to properly consider a further aspect which is the RT technological advancements which has occurred over the years allowing innovative surgical approaches and newly developed drugs which has led to a significant narrowing of RT indications as alternative strategy.

Results

We present here the findings regarding the most relevant surveys and national guidelines identified about the clinical indications for RT in benign disorders.

The largest worldwide survey available was promoted in 1998 by the European Society for Radiotherapy and Oncology (ESTRO) and produced a list of the 28 most common benign disorders commonly treated by RT during la last decade of the past century. The results of the survey highlighted great variability regarding both the indications and the RT schedules used across the 508 participating centers. Such significant differences in the clinical patterns of practice were astonishingly mainly related to the different geographical origin of the countries where the centers belonged.

A few years later, in 2001, another important survey was conducted in the United States of America about RT indications and treatment programs ongoing in the country and the authors concluded that many earlier indications of RT for benign diseases had been supplanted by modern medical therapies and new surgical approaches.

An additional source of data comes from the Royal College of Radiologists that launched in 2015 a detailed survey about the use of RT for benign entities in the United Kingdom. In contrast to previous surveys, in this issue the authors organized the results according to the primary anatomical sites involved (e.g., eye, bone, head and neck, skin, brain) managing to identify 17 benign conditions in which RT is still indicated in UK centers.

The most active community of radiation oncologists using RT for benign diseases is historically based in Germany; the German Cooperative Group on Radiotherapy for Benign Diseases has produced over the years several guidelines about the role of RT in benign diseases[,,,].

The strikingly interesting approach which has been used by the German researchers is to identify the diseases not just on anatomical basis but identifying four main categories: degenerative diseases, hyperproliferative diseases, functional diseases and stereotactic indications.

In order to complete this brief overview, it is mandatory to add a few more uncommon and recent indications which are also present in literature: in detail they are about the role of RT in the management of coronary stent restenosis and refractory ventricular tachycardia.

A summary of the main contemporary indications with the relative doses is reported in Table I.

Discussion

Some major points need to be addressed after the results of the surveys presented so far.

In fact, even though the number of patients affected by benign diseases treated by RT so far may not negligible, there are several reasons why still no uniform consensus has been so far reached across international scientific societies.

First of all, there is a great variety of benign entities with no uniform and commonly shared nomenclature. This lack of uniformity makes it difficult to compare the results of the different disorders. In addition, there are no universally accepted categories to group or frame such conditions together.

In some situations, there is not even a well-defined distinction between benign and malignant disease presentations, such in the case of the angiofibroma of the nasopharynx[3].

Another point of paramount importance which needs to be considered is that RT represents just alternative to medical or surgical treatments for benign conditions. As suggested before, however, over the last decades both surgical techniques have enormously evolved, and new drugs have been approved for their efficacy in the management of several conditions[2]. This combination has significantly narrowed the clinical indications for RT.

A particular consideration needs to be done especially when considering pediatric patients. The use of ionizing radiations, in fact, in this context should be considered only in very exceptional cases and only after careful evaluation of all the pros and cons especially with the possible occurrence of late side effects according to the anatomical site treated.

In particular, the possible risk of radiation-induced second tumors should be carefully considered. In fact, evidence gathered from nuclear acci-

Table I. List of main benign diseases treated by radiotherapy in current clinical practice.

		Functional category			
		Degenerative	Hyperproliferative	Functional	Focal lesion
Anatomical site	Eye		Pterygium	Graves' disease Orbital pseudotumor	
	Head and neck			Sialorrhoea	Paraganglioma
	Skin		Keloid*	Lymphatic fistula	
	Brain				Arteriovenous malformation Meningioma Acoustic neuroma Pituitary adenoma Trigeminal neuralgia
	Bones and joints	Arthritis tendinitis	Dupuytren's disease Ledderhose's disease	Heterotopic ossification	
	Heart and peripheral vascular system			Coronary stent restenosis* Vascular stent restenosis*	Refractory cardiac arrhythmias
Dose range (Gy)		2-8	3-30	6-40	12-60

*Elective indications for IRT.

dents and from large populations-based registries, has shown that radiation-induced tumors typically may develop many years after the irradiation, even after decades after the initial exposure.

A critical point to address is the specific RT technique used in this setting of benign diseases. In fact, RT may be delivered either as external beam RT (ERT) or as interventional RT (IRT, Brachytherapy). IRT has several advantages over ERT because of its rapid fall-off of the dose, which allows sparing better the organs at risk (OARs) and the surrounding tissues and in highly selected might represent a valid alternative for surgery, especially in anatomically delicate or particularly exposed sites. Recent technological advancements, such as the introduction of hybrid MR-linear accelerators have however enhanced the possibility to safely deliver the prescribed dose, efficaciously sparing the nearby OARs also by using ERT.

Conclusions

RT is a feasible therapeutic strategy for benign diseases, especially after medical therapies have failed, because it allows to treat several invalidating conditions potentially avoiding major surgical procedures. A careful evaluation in selecting the indication is essential and all the choices should be thoroughly discussed with the patients.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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