A Data-Based Approach to a Keloid Post-Excisional Radiotherapy Treatment (PERT) Pathway

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Background

A 2017 meta-analysis of 62 studies (27 superficial X-ray; 18 electron beam; and 17 brachytherapy) of keloid post-excisional radiotherapy treatment (PERT)concluded that, regardless of type of radiation employed, a recurrence rate of approximately 20% was achievable and that PERT was superior to radiation monotherapy (ref. 1). However,a subsequent Report of the 3rd International Keloid Symposium (IKS) in Beijing in 2019 identified that "the biggest obstacle to the development of optimal treatment for patients with keloids is the lack of data-driven treatment pathways" (ref. 2).

In 2022,Guidelines from the German Society for Radiation Oncology (DEGRO)approved radiotherapy after surgical intervention as a viable option for keloid treatmentbut only at Evidence Level 4 (Case Series), due to a lack of Evidence Level 1 Randomised Controlled Trial (RCT) data. DEGRO also advised that keloid radiotherapy as a monotherapy be only employed exceptionally (ref. 3). However, by 2025, only 4 registered keloid treatment research studies (3RCTs & 1 Cohort Study) were ongoing, none evaluating PERT (ref. 4).

To overcome this apparent lack of progress, this study aims to consider a novel approach to the analysis of PERT Audit outcome data presented at the 2nd, 3rd & 4th IKS (refs.5, 6& 7), with a view to re-formulating it as Evidence Level 2 Cohort Studies.In turn,this evidence will facilitate optimisation of aradiotherapy treatment dose regimen for PERT, as well as the development of a related optimal treatment pathway including a cost-effectiveness perspective. The applicability of this study approach to other keloid treatment modalities, e.g. laser therapy, cryotherapy, etc. will also be briefly considered.

Method

Historically, untreated keloid tumours are characterised by infiltration into surrounding normal tissue, progression over time and only rare instances of regression. As a result, virtually all untreated keloids will either remain stable or continue to grow (ref. 8).

Given this predictable behaviour, it can be argued that within the population of untreated keloids, a suitable comparator cohort can be identified to match any patient cohort in a

keloid Audit study. This matching can be based on factors such as keloid location, stage, patient age, gender, and ethnicity. Consequently, long−term outcome Audits of treated keloid patients can be considered Cohort Studies, qualifying their outcome data for Evidence Level 2 classification (ref. 9).

Applying this approach to control groups, the three previously referenced KFS Audits can be regarded as Cohort Studies. Data from these Audits will be analysed to assess treatment outcomes, then cross −referenced with radiobiological data to determine the optimal treatment regimen. Following this, the treatment equipment used will be evaluated for cost−effectiveness, ultimately informing the proposal of an optimal treatment pathway.

Results

Treatment outcome data inrefs. 5, 6 & 7(now seen as Cohort Studies):

Centre Location	Treatment Unit; kV or MeV	Treatment Dose (Gy); No. of fractions(#)	No. of Keloids or Patients	Recurrence Rate; Mean Follow-Up	Adverse Effects
Beijing, China (ref. 6)	Linear Accelerator (Linac); 6 or 7 MeV	18Gy/2#; #1w/in 24h-48h;& #2 1wk later	834 keloids	9.6%; 3.3 years	9.8%
Nairobi, Kenya (ref. 7)	SXRT Unit: e.g. 100kV	12Gy/1# w/in 24 h	523 patients	10.0%; 5 years	None "long term"
London, UK (ref. 8)	SXRT Unit: e.g.100kV	10Gy/1# w/in 24h	(80†; 102) 182 keloids	16.0%†& 14.7%; 5 years	Minimal side effects

No radiation induced cancers observed in any of the studies; †study published in 2003

Optimal patient outcomes were observed for a dose of 10Gy to 12 Gy of X −rays delivered as a single fraction within 24 hours of keloid excision. Treatment by electrons in 2 fractions, each of 9Gy, did not improve the recurrence rate but increased adverse effects significantly.

An alternative approach is to apply the LQ radiobiological model to calculate the radiobiologically effective dose (BED) and produce a BED comparison of single fraction treatment doses with their reported clinical implications. Using the BED formula:BED = nxd[1+d/(α/β)], for keloids α/β=2 to 3 and, using 2.5 (ref. 10):

Single Fraction Dose	$BED_{2.5}$(Gy)	Clinical Implications
8 Gy / 1#	33.6 Gy	Effective, lower toxicity but potential increasing recurrence risk
10 Gy / 1#	50.0 Gy	Higher effectiveness but fibrosis risk
12 Gy / 1#	69.6 Gy	Significantly higher BED, higher risk of fibrosis & poorer cosmesis

On these bases, an optimal treatment pathway would include an optimsed dose protocol of 10 to 12 Gy/1#, treated within 24 hours of keloid excision @ 100kV (with a higher kV for thick keloids and a lower kV for thin keloids).

A cost−effectiveness analysis of treatment pathways employing an SXRT unit or a linac for benign disease treatment, has shown that SXRT units are around 10X cheaper to purchase and 10X cheaper to maintain. The construction cost of a lead lined SXRT treatment room is also significantly less than that of a concrete bunker for a linac. Finally, physicist (dosimetry & QA) and radiographer (treatment) staffing costs are lower for an SXRT unit than a linac (ref. 11).

Conclusions

As nearly 100% of untreated keloids stabilise or progress, well structured long−term treatment outcome Audits can be viewed as Cohort Studies qualifying their outcome data for Evidence Level 2 classification

Keloid treatment outcome data and radiobiological calculations both suggest that a single 10−12Gy treatment fraction within 24 hours of surgery is the optimum dose for PERT for optimisation of recurrence and adverse effect rates. This also suggests that when 2 x 9Gy treatment fractions are employed, the second fraction may be unnecessary and only serve to increase the probability of adverse effects.

A quoted cost−effectiveness analysis showed that using an SXRT unit,as part of an optimal pathway for effective keloid management,was cost−effective compared with using a linac,

Ongoing data collection, involving routine auditing and collation of a range of parameters, preferably in a standardised format,is crucial for further refining data−driven radiotherapy treatment pathways for keloids,

Adopting a similar outcome data recording framework for treatment modalities other than radiotherapy, e.g. laser therapy, cryotherapy, etc., would facilitate comparison of outcomes and development of data–driven optimisation of treatment for each modality. In turn, inter–modality comparison of optimised treatment modalities could then be undertaken.

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