

Exploring the Patient Perspective of Bone Sarcoma Survivors Who Have Undergone Particle Radiotherapy Abroad

LENA FAUSKE^{1,2}, NINA L. JEBSEN^{3,4}, HILDE BONDEVIK² and ØYVIND S. BRULAND^{1,5}

¹Department of Oncology, Norwegian Radium Hospital, Oslo University Hospital, Oslo, Norway;

²Department of Interdisciplinary Health Sciences, Institute of Health and Society, University of Oslo, Oslo, Norway;

³Department of Oncology, Haukeland University Hospital, Bergen, Norway;

⁴Centre for Cancer Biomarkers (CCBIO), University of Bergen, Bergen, Norway;

⁵Institute of Clinical Medicine, University of Oslo, Oslo, Norway

Abstract. *Background/Aim:* Sarcoma patients' experiences of their health-related quality of life and late effects following particle therapy are sparse. Such knowledge is essential to optimize treatment compliance and follow-up care related to this rapidly developing, but still centralized treatment modality. *Patients and Methods:* This qualitative study has an explorative design and applies a phenomenological and hermeneutical approach based on semi-structured interviews with 12 bone sarcoma patients who had undergone particle therapy abroad. The data were interpreted using thematic analysis. *Results:* Several of the participants called for more information about how the treatment would be carried out, its acute side effects and late complications. Most participants had positive experiences from the treatment and their stay abroad, but several struggled with late effects and other challenges. Themes that emerged from the analysis were "importance of being prepared", "treatment and stay abroad", "basically healthy, but with health problems and challenges". *Conclusion:* Oncologists who inform and refer patients to particle therapy abroad must have sufficient experience of this treatment modality, prognoses, acute side effects, and late complications. Findings derived from this study may improve treatment preparation and compliance, enhance understanding of individual patient challenges to reduce stress and worry, and lead to better follow-up care and consequently quality of life of this selected group of bone sarcoma patients.

Correspondence to: Lena Fauske, The Norwegian Radium Hospital, Oslo University Hospital, Ullernchausseen 70, 0379 Oslo, Norway. Tel: +47 22934000, e-mail: lena.fauske@ous-hf.no

Key Words: Bone sarcoma, particle beam therapy, protons, carbon ions, qualitative research.



This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY-NC-ND) 4.0 international license (<https://creativecommons.org/licenses/by-nc-nd/4.0>).

Sarcoma survivors frequently struggle with late effects of treatment (1-4). The literature is sparse on their experiences, their health-related quality of life and late effects following particle therapy (5). Only one quantitative article on sarcoma patients was identified in which Srivastava *et al.* (6) studied chordoma and chondrosarcoma patients and concluded that their quality of life was not adversely affected during treatment, which allowed them to enjoy a normal life despite the lengthy treatment. No qualitative studies involving patients' own narratives have been found for these diagnostic groups of bone sarcomas. However, limited qualitative research has been published on the perspectives of patients treated with protons for brain cancer (7, 8), and relatives' perspectives on proton treatment given to pediatric cancer patients (9, 10). Living in a hotel, often alone, during treatment has been reported as an additional challenge by patients with primary brain tumors being treated with proton therapy far from home (8). Patients experienced an ongoing process in which they made several adjustments to cope, enhance their well-being, and manage the altered social context (8). Furthermore, concerns about diagnosis, treatment, and symptoms, in addition to spending time away from home, represent a significant additional burden for both patients and their family members (10).

Particle-beam therapy is of increasing clinical use primarily due to its physical characteristics with improved dose distributions, and also related to more recent digital and technological improvements implemented in available equipment from commercial suppliers (11-14). Particle beam treatment, most often as proton therapy, is provided in centralized facilities. Among adult patients, major differences exist between countries regarding indication for, referral to, and delivery of such treatment (14). Dose conformity of protons and carbon ions allows for radiation dose escalation in the defined target volume to improve local tumor control of more resistant cancers, as well as sparing of normal tissues to reduce the risk of radiation-related sequelae and secondary malignancies (15, 16). However, the shift from

photon therapy to particle therapy could be associated with unexpected toxicity due to the impact of uncertainties regarding dosimetric variations (17-19), for example within the spread-out Bragg peak or due to organ movements, air-filled cavities, or prosthetic implants. Thus, long-term follow-up of patients treated with particle-based radiotherapy is crucial. Compared to the best photon-based conformal radiotherapy available (20), the dosimetric advantages offered by protons have recently been shown to reduce treatment-related toxicity in patients undergoing radiochemotherapy at various anatomical sites (21).

Bone sarcomas comprise a group of rare cancers that include some of the few entities for which particle-based radiotherapy has emerged as standard indications and the treatment of choice (11, 14, 22), such as skull base, spinal and pelvic chondrosarcomas and chordomas (23-26). Carbon ion treatment is shown to be effective for bone and soft tissue sarcomas of the head and neck with adverse events within the expected range (27). In addition, patients with axial osteosarcoma, Ewing sarcoma or other childhood sarcomas, such as rhabdo-myosarcoma (22), are increasingly being given proton therapy as the preferred local treatment modality. Nevertheless, extensive surgery remains the principal treatment modality for bone sarcoma, supplemented by chemotherapy and/or radiotherapy tailored to tumor type and prognostic factors (28).

Using a qualitative methodology, we have attempted to learn more about the experiences of selected bone sarcoma patients referred for particle beam therapy given abroad in terms of communication, treatment, and acute side effects, in addition to the patients' psychosocial experiences during their stay. The current project aimed to explore the patient perspective on how information from Norwegian healthcare professionals was provided and perceived regarding prognosis, treatment indication and its effect, preparation for what to expect during the treatment process, and side effects in a short-term perspective. Furthermore, we have attempted to gain knowledge about the long-term effects of the treatment, and communication during the follow-up period.

Patients and Methods

We used an exploratory qualitative research design involving a phenomenological and hermeneutical approach to analysis. In qualitative research, phenomenology is a perspective that indicates an interest in understanding phenomena from participants' own perspectives and describing the world as it is experienced by them (29). This form of research has a strong focus on reflective interpretation, and description is inextricably linked to interpretation and hermeneutics (30). Comprehension involves the preunderstanding of both participants and researcher, as well as the context, and it develops throughout the research process (31). Using this qualitative method, we expected to gain knowledge of individual experiences of medical and psychosocial challenges related to proton and carbon therapy and the associated stay abroad.

Identification and selection of patients. Following a multidisciplinary sarcoma team evaluation at two university hospitals, Norwegian Radium Hospital, Oslo University Hospital (NRH OUH) and Haukeland University Hospital (HUH), bone sarcoma patients who fulfil the criteria for particle-based radiotherapy have for several years been sent abroad for treatment since no proton facility exists in Norway. This treatment is fully paid for by the Norwegian national healthcare system.

The participants in the project were recruited from NRH OUH (n=8) and HUH (n=4) and included seven women and five men aged 14-56 years at diagnosis. Time from primary diagnosis ranged from two to 16 years, with a median of 5.8 years. Participants were referred to and treated with proton (n=9) or carbon ion (n=3) therapy in Heidelberg, Germany from 2014 to 2022 (Table I). All participants in this study were considered cured or in long-term stable clinical and radiological remission. They all had regular follow up at the sarcoma outpatient clinics of the NRH OUH and HUH in line with routine guidelines. Six had undergone surgery as primary treatment and one with only a de-bulking operation. One patient with Ewing sarcoma received adjuvant chemotherapy before, during and after proton therapy (Table I). All patients had a short trip to the University Hospital in Heidelberg for dosage planning and mask fitting before returning to undergo therapy. All participants stayed in a hotel during the particle beam treatment. In the results section of this paper, as well as in the tables, the participants are identified as P1-P12.

Procedure. Experienced sarcoma oncologists at the NRH OUH and HUH identified and contacted potentially eligible participants (n=12) for information and possible recruitment. All were willing to consider participating in the study and were sent an information letter including a summary of the background and purpose of the project and the study procedures. These 12 agreed to participate and received a phone call from the first author to arrange a date for the interview. They were informed that neither consenting to nor declining participation would affect their routine follow-up care and that they were free to withdraw from the study at any point. A signed informed consent was obtained before the interview, based on the "Information Sheet for Adults" template provided by the Norwegian Regional Committees for Medical and Health Research Ethics.

The data protection officers of the NRH OUH and HUH approved the study (approval numbers 21/26477 and 2022/3466). In accordance with the principles of ICH-GCP 2.1-2.3, the foreseeable risks, inconveniences, and patient rights associated with the project were evaluated. A sarcoma patient advisory group was involved in the planning of the study and recommended the protocol.

The first author conducted the interviews during a routine clinical follow-up appointment at the NRH OUH (n=4), in a participant's office (n=2), or by phone (n=6) due to COVID-19 or a long travel distance. The interviews lasted from 44 to 105 minutes with an average of 64 minutes and were later transcribed verbatim by a medical secretary. The participants were invited to narrate their story from their diagnosis, via the decision to recommend particle therapy, to treatment and follow-up. An interview guide was used to explore how the patients found the information they received about their planned treatment and prognosis, including the justification for and choice of treatment, and its side effects, as well as to investigate the patients' perception of their journey and stay abroad. The study also recorded the participants' subjective reporting of their quality of life and late adverse effects following

Table I. *Clinical information on the 12 participants.*

Participant	Diagnosis	Anatomical location	Years since diagnosis	Primary treatment	Post-operative particle therapy	Definitive particle therapy
P1	Chordoma	Clivus	7	Surgery	Protons	
P2	Chordoma	Clivus	4	Radiotherapy		Protons
P3	Chondrosarcoma	Temporal bone and clivus	5	Surgery	Protons	
P4	Ewing sarcoma	Ileum and sacrum bones	3	Chemotherapy		Protons
P5	Chordoma	Cervical spine C5	4	Surgery	Carbon ions	
P6	Chondrosarcoma	Clivus	8	Surgery	Protons	
P7	Chordoma	Sacrum	2	Radiotherapy		Carbon ions
P8	Chondrosarcoma	Petrous bone	7	Radiotherapy		Protons
P9	Chondrosarcoma	Skull base	8	Surgery	Protons	
P10	Chondrosarcoma	Left temporal bone	6	Debulking surgery	Protons	
P11	Chondrosarcoma	Mediastinum (trachea)	5	Radiotherapy		Carbon ions
P12	Chondrosarcoma	Clivus/cavernous sinus	3	Surgery	Protons	

treatment, in addition to examining their views on the follow-up care provided at the sarcoma outpatient clinics. All the information collected was stored in line with the institutional data protection policy, and the transcripts were de-identified.

Analysis. We used reflexive thematic analysis (32, 33) to identify patterns of meaning across the dataset to answer the research questions. These patterns were identified through a rigorous process of data familiarization, data coding, theme development, and revision. The entire dataset was coded in detail by hand by the first author. The codes were then divided into categories, themes, and concepts (33) and discussed by all the authors. Throughout the analysis, the researchers regularly returned to the original data to check the themes and quotes and ensure that the meaning had not been lost during interpretation or translation (29, 33).

Results

By exploring trajectories of included bone sarcoma patients receiving particle therapy abroad, themes extracted from the analysis were “importance of being prepared”, “treatment and stay abroad”, “basically healthy, but with health problems and challenges”. Selected quotations from the interviews in relation to various themes and sub-themes are presented in Table II.

The importance of being prepared. Only four of the 12 patients undergoing radiotherapy in Heidelberg reported being very satisfied with their communication with doctors in Norway prior to the referral. This implied that information about treatment, prognosis, potential side effects and late complications was regarded sufficient for these patients. The other eight mentioned insufficient or no information in one or more areas, which gave rise to uncertainty and insecurity throughout their trajectory. Several stated that they did not know what to expect when they travelled to Heidelberg and would have liked to be better prepared. Two pointed out that they themselves had to obtain additional information about the treatment. One also had to take the initiative on which

treatment she should receive. Despite partly lacking information, three of the eight mentioned that they felt well taken care of and safe in the process before the therapy. Half of the participants pointed out that they were not included in the actual decision-making process regarding the choice of treatment, but that they had no complaints about the decision to recommend particle radiation. Many expressed gratitude for the opportunity.

The 12 participants had been examined and diagnosed by various doctors at the two university hospitals in Norway. Only a few of these doctors had good knowledge and experience of sending patients abroad for particle therapy since this was a rare event. Several participants wanted more advance information about how the treatment would be carried out. Of those who had bone sarcomas in the head and neck region (n=8), several said that fitting and wearing the mask was a very unpleasant experience that they were unprepared for, and they would have liked prior information about this. The fact that they were completely unprepared represented a bad start to their treatment. More detailed and personalized information about what would happen to them during treatment, as well as prognosis of survival and what they could expect from side effects and late effects, was highlighted as important for feeling safe and satisfied throughout the trajectory.

In conjunction with a long stay treatment abroad, there are usually considerable financial and administrative preparations to make. With one exception, the participants pointed out that travel and accommodation were arranged in an excellent manner by the International Office. The participants themselves had neither work nor personal expenses related to the treatment, travel, and accommodation. Accommodation for a relative was also granted if deemed necessary. All participants were very satisfied with the hotel and the neighborhood. A couple had to change hotels at the start and were very satisfied after that.

Table II. *Selected quotations from the interview.*

Themes/subthemes	Selected quotations from the interviews
Information prior to treatment	I felt I didn't get enough information, I would have liked to get more (...) about the place I was going to, what to expect, what the treatment's like there, I knew I'd have radiation for a certain period, but it would have been nice to know what would happen on those days. (...) I wasn't prepared for the mask either. P6
Information	The doctor said: "You have to decide about this yourself", but I think I was really like, do whatever's best, and I felt a lot of trust and I was very calm, he was very good at explaining and telling me and asking if there was anything else I wanted to know, so I really felt that I was involved in the decision, I could have said I didn't want to do it. P3
Prognosis	I understood that it (proton radiation) could be a very good alternative, especially considering that there was such a big risk involved in surgery, so then it was a very easy decision for me at least. (...) And the fact that people who've had that treatment before have had very, very good results. P4
Side effects	The first time I heard anything about the prognosis, I don't know if it was a nurse or a doctor down there in Heidelberg who said it halfway through the treatment, then I was told: "This treatment is very good and 90% of the patients who have had the treatment haven't had a relapse for five years". P9
Late effects	No, they didn't say anything about my prognosis. I asked several times: "So what are my chances with this treatment?" and so on. I'd say there was very little information about my future health prospects. No one was willing to say anything, even though I told them that not knowing made me unsure of things, it's hard to go around with that uncertainty. (...) Some advice about what to expect and when, that type of thing. P10
Organizing the treatment abroad	I got a lot of good information about the journey and accommodation there. (...) And the travel coordinator sorted everything out and called me to say: "Now you have to go there and now you go there", so it was really great. She arranged everything from the moment I arrived in Frankfurt. P1
Travel, stay and accommodation	I was told early on that there was a foreign travel department (International Office) that took care of all the practical details of arranging your trip and your stay there. That worked very well. They even said I could take someone with me. (...). There were no extra expenses and as far as I can remember. P7
The treatment given in Heidelberg	Yes, well, some of the side effects during treatment I've mentioned are nausea, mucus in my throat, hair loss, sunburn, and fatigue. I had a doctor available when I started the radiation, and also for regular monitoring during my stay, that was appointments. It was a different experience to be treated in the German system compared to the Norwegian one, but of course it was in a different situation and setting. (...). But the flexibility of the German system, I think that's an example to follow. P10
Side effects during treatment	Before the treatment things were fine, but when I got up onto that table where I was lying, I felt totally knocked out afterwards. (...) I had no strength. No, it wasn't directly painful (getting radiation), but it sort of drained my strength. (...). And then it was a real struggle for me to make it back (to the hotel) (...). Then I really needed to relax. And then a bit later in the evening it was time to have something to eat. P11
	When you get to that hospital (in Heidelberg), it's 100% German, so you don't understand anything if you don't know German. And then you have to find your way through those corridors and the hospital staff only speak German. (...). The doctors speak English (...) I could talk to them. P8
	I was surprised how good it actually was. I didn't notice anything after the treatment. (...). The only thing I noticed for a few days was a kind of chlorine sensation from the smell of chlorine in my nose. (...). I was just extremely lucky. There were no signs of any of the side effects that they mentioned to me. I joined the fitness centre down there and worked out four or five days a week I reckon, strength training. And I rode a bike to and from the hospital during the treatment. P9
Life during stay in Heidelberg	I think maybe out of all the seven weeks, I was alone for one week altogether. My friends and my mother came to see me, there was always someone there. That was a must. And very nice.
Social activities	I think I'd have been very, very lonely if that hadn't happened. P8 (On a good day): I might take the tram down to town and then walk around there a bit and I might sit in a café and have a coffee and I'd kind of react a bit more to sounds and noise and things around me. Then I felt like I had a little more energy. And I also noticed that when I'd had a visit, I felt worn out afterwards. So, then I needed a few quiet days. P3 Well, a bad day was when I came back from treatment and I couldn't get up again, because I was so exhausted. I couldn't make myself anything to eat, I just lay there. P11 It was July or August, and the weather was fine, so it was just like a holiday for us. We borrowed bikes and cycled around a lot. (...). We went miles and miles on our bikes, on several days. (...). And as the radiation therapy lasted a long time, it was good to have someone with me. Yes, I think I might have got a bit lonely there by myself. P7

Table II. *Continued*

Table II. *Continued*

Themes/subthemes	Selected quotations from the interviews
Life after treatment	I had a hard time. For a number of years, I couldn't work. I've felt really exhausted and
Sub-acute effects	I think some of it was anxiety, actually. Not just fatigue. P10
Late effects	I live more or less the same life as I used to before, it's just that I definitely don't have the same energy. P4
Vocational life	No, I'm not the same person I used to be. (...) Then I was like full of life and went places with everyone, and everyone came here. (...). So I'm not so sociable as I was. P11
Social life	I was young, you know, so I'd expected to be exactly the way I was before I got sick and I thought I'd get well, you know. I didn't imagine that late effects would crop up. P12
Existential life	I'm not afraid of dying. (...) I don't have those deep, painful, difficult thoughts about 'Why?' and feeling bitter and being afraid and so on, I'm not like that. I feel more happy that I'm alive, that's how I feel. P3 I don't have time to worry about me. I'm functioning just fine. So it's just a matter of making our life as good as it can be. So I'm not worried about my own health, in fact. No, I'm not. Except that I have to be careful not to get burned out. P5
Long-term follow up at out-patient clinics	A bit more information maybe, not just stuff like "You look fine, do you have any questions?" Preferably more like "Yes, it (the tumor) looks fine, it hasn't got any bigger, it might not have got any smaller or it was that big last time we did an MRI scan and that's how big it is now, and we think that in the future it might be that size". (...) Now I feel like I'm in a bubble, I don't know what's going to happen, whether the symptoms will continue until it gets smaller or if it will still be pressing on the same nerves or what can I do then. Because I've lost my job. I'm afraid of making a big effort to get a new job or I'm afraid of getting very tired because then the symptoms will come. And what should I do in the future? P2 There was also a period when I had a lot of anxiety, and it was partly caused by the hospital (in Norway) because I asked them for answers, I asked for something specific and I got nothing. (...) And even if they don't have a definite answer, it's important that they tell you some things when you keep on asking. P10 Well yes, I felt that it (the polyclinic) was professional. I have confidence in their skill. I feel they know what they're doing (...) and I have a good dialogue with them. I've had various doctors who have called me and followed me up through these almost eight years, but I think they all explain things well. And they're actually personal. P6

The treatment and stay abroad. The stay in Heidelberg was for nearly all (n=11) a positive experience. Professional implementation and helpful information about the course of treatment and side effects when they arrived at the hospital in Heidelberg meant that most participants had a positive experience of the treatment despite some language problems and the fact that they were far from home. A few pointed out that there could be some delays and waiting in connection with the radiation, but this was manageable. Several emphasized that they also received good care from healthcare personnel if they experienced side effects from the treatment.

Reduced physical performance and treatment side effects negatively affected activity during the stay in several of the cases. Some were very active and sociable and often went out. They exercised at the hotel and had energy to go sightseeing in the area, whereas those impaired by previous or current treatment mostly stayed at the hotel resting. Five of the participants stated that they were in good shape with few or no side effects while the treatment was ongoing, while the other seven said that they had varying degrees of tiredness and fatigue, which affected their activity level. Other side effects that persisted throughout the treatment were nausea, dizziness, sore throat, loss of taste, decreased

appetite and hair loss at the radiation site. Radiation toxicity to the skin and impaired hearing or memory were also mentioned. Many reported a mix of good and bad days. A bad day consisted of lying on the sofa, whereas a good day was filled with activity and socializing.

Most of the participants received visitors during their stay and emphasized that this was very important for their perceived security and well-being and that it helped the time pass during the weeks they stayed in Heidelberg. For those who were in bad shape during the treatment, it was important to have relatives/visitors who could cook and help with practical matters. One of the participants received chemotherapy during the treatment and six had relatively recently undergone surgery before coming to Heidelberg, which probably impaired their health during their stay.

Basically healthy, but with some health problems and challenges. Seven of the 12 reported several late effects and challenges after particle therapy. As mentioned above, six participants had undergone one or two operations before the radiotherapy, which for several also contributed to late effects. Given the different localizations of the tumour, the participants' complaints and life after treatment varied.

Fatigue, tiredness, and reduced energy arose in nine of the participants in the months after treatment. For some, this gradually passed after a few months or years, and they were able to return to work or studies. Seven of these nine participants were working full-time at the time of the interview, but several emphasized that they still struggled with fatigue and other late effects. Furthermore, one was still on sick leave five years later, three were on disability benefits and one was a pensioner. Those with fatigue pointed out that they had a restricted social life, they were less physically active, and that fatigue affected their ability to work. Some said that working full-time was demanding and interfered with their social life. Three said that they had suffered a great deal from anxiety and depression because of the disease, which they would have liked more help to deal with. Many pointed out the strain of being uncertain and unable to receive adequate information and answers about whether they were healthy or could expect a relapse. Despite this, most considered themselves to be healthy, but with some problems and challenges.

All participants had regular follow-up visits at the NRH OUH or HUH sarcoma outpatient clinics. Eight out of 12 participants said that they were satisfied or very satisfied with these. However, four had received little or no help from the healthcare system. Eight of the 12 said that they had requested help to deal with side effects, including fatigue. Two of these eight had received good help, three had received some help, while three complained that they had received no help at all. One pointed out that she only received good help not before she got a new doctor after a few years. Several of the patients had complex challenges due to both the disease and treatment, especially those who had undergone prior surgery. Information about future health prospects, help to cope with fatigue and anxiety, and challenges with balance and impotence were some of the inadequacies or late effects they missed talking to the doctor about and getting help to deal with.

Discussion

In Norway, fewer than ten sarcoma patients are sent abroad each year for particle-based radiotherapy. Several doctors, both oncologists and orthopedic surgeons, decide on an interdisciplinary basis on the recommended treatment and inform the patient. The oncologists who refer patients to particle therapy abroad will not necessarily follow them up afterwards at the outpatient clinic. With so few patients involved in this study, it was possible to consult the medical records to see which doctors had informed the patients. There turned out to be consistency between patients who felt that they received adequate information before the treatment abroad and good follow-up care afterwards and a high level of experience in particle therapy of the doctors involved. A

qualitative study of parental views on treatment and information sources in child proton beam therapy (9) confirms the challenge related to 'fragmented expertise' that comes with the 'novelty' of the radiation therapy, the rare nature of the tumors, and the remote location of the particle treatment facility. This is clearly in line with the findings in the current study.

This study revealed a gap between information provided by clinicians as perceived by the participants and knowledge about their upcoming treatment abroad, which they later considered crucial. This included individual prognoses following particle therapy and possible acute and late side effects to ensure that the participants could feel safe and satisfied throughout their trajectory. Although a few were satisfied with the communication and support from the Norwegian healthcare system, several mentioned uncertainty, frustration, and unpleasant experiences. This may be related to the fact that particle therapy is a highly specialized treatment that many doctors know little about. In addition, the treatment takes several weeks, far from home and in a country with a language unfamiliar to most Norwegian patients. Some also suffered from anxiety and depression later during their trajectory. This may partly be due to poor information about the prognosis and inadequate care for late effects.

Several patients with head and neck sarcomas commented that the mask was an unpleasant experience that they would have liked to be better prepared for. When other patients, such as those with head and neck carcinomas, are given radiotherapy in Norway, radiation therapists are involved and provide information about the mandatory use of a mask before treatment. This was not the case with our patients, and they arrived unprepared for this mandatory part of the treatment in Heidelberg. Although several pointed out that they got used to the mask after a while, it was an extremely unpleasant experience and a bad start, which could have been avoided if adequate information had been given in Norway beforehand.

An oncologist who neither has practical experience nor detailed knowledge of the proton or carbon therapy center abroad can hardly inform and prepare patients adequately. Furthermore, the referring oncologists have little or no contact with patients during the treatment (which lasted from two to seven weeks in Heidelberg for our participants). Lastly, with little prior experience of follow-up at the outpatient clinic for this category of patients, they cannot in a sufficient manner inform newly diagnosed patients about the treatment and possible late effects.

Although the stay in Heidelberg was experienced differently by participants depending on the degree of side effects and their physical condition, it was in general a positive experience to stay in the city and at the hotel. This was because all practical matters were clarified and arranged by the

International Office in Norway. Being able to travel with a relative was also felt to be essential for some of those with side effects and fatigue during their stay. Most adapted well to life and a different social context. One of the reasons for this was having visitors for part of their stay. Our participants underlined that close relationships with their children, family or friends gave them the strength to struggle through. It is important that patients receiving treatment far from home find a way to remain a part of their family and maintain a feeling of belonging despite the altered social context (8).

The treatment at the hospital in Heidelberg was described in positive terms by most participants. Many said that it could be difficult to find one's way in a large hospital as all information was in German and most health personnel, except for the doctors, spoke little or no English. The treatment itself was professional and effective. Several of our participants experienced side effects during treatment, with fatigue being the most pronounced. Fatigue is one of the most common side effects in patients with cancer (34). In a quality-of-life study (6), 35% of the patients that underwent proton treatment experienced worsening fatigue, whereas in our study 7 of 12 said they had varying degrees of fatigue during treatment.

Norwegian sarcoma patients receive ten years of systematic follow-up after treatment. Our study shows that this does not necessarily capture essential needs or provide adequate support for several of those treated with protons or carbon ions. Most patients eventually realized that abnormal or residual findings on radiographs were assumed to be harmless. Frustration was therefore mostly about physical and psychosocial problems and the future outlook for those who had long-term challenges. In an older study (35) of 101 cancer patients, almost all participants expressed a general need for as much information as possible, regardless of whether it was good or bad. Baile and Aaron (36) report that most cancer patients require substantial emotional support and a high level of information about their disease. Even when motivated, patients often find it difficult to obtain timely and correct information, which may lead to dissatisfaction and misinformation about their illness. Doctors neglect opportunities to respond empathically to patients' concerns and ignore their desire to discuss health-related quality of life issues (37). A few of the participants in our study pointed out that a lack of information about their prognosis created and maintained frustration and anxiety years after the treatment. Two of the patients in our study underlined that even if a priori information was not emphasized, it seemed of great importance to patients that their questions were answered with as accurate information as possible.

A quantitative study (38) underlined that information for cancer patients could be better tailored to meet patient preferences. One strategy is to develop survivorship care

plans for patients and their family doctors that include information about the specific type of malignancy, ongoing treatment options, follow-up examinations, and other individualized information. Doctors could also provide patients with a list of trusted websites that contain appropriate information or develop secure patient information portals with access to information specific to the individual patient's malignancy (38).

We recognize that the relatively low number of highly selected and motivated bone sarcoma survivors involved in this project represents a limitation. Nevertheless, in qualitative research, we do not seek to gather representative data, but rather to illuminate the phenomenon as experienced by the participants from their own perspectives.

Several patients in our study who had undergone both surgery and particle beam radiotherapy experienced subjective challenges related to late treatment complications. Unfortunately, the design of the current study cannot separate the contribution of each treatment modality and the impact of the combination. Currently, there is a trend in the sarcoma community to recommend definitive particle radiotherapy as the local treatment modality of choice at primary diagnosis for the majority of axial bone sarcomas.

There are around 100 proton therapy centers world-wide, most started in the last decade and several more under construction (39, 40). However, several countries will, most likely, not build their own and have to collaborate at an international level. Chordoma patients may still best be treated with definitive carbon ion therapy. The findings in the current study may have relevance for the various proton centers existing or currently under construction around the world in terms of the potential for improved preparation and information of bone sarcoma patients prior to referral. We also believe that our findings may have relevance for patients with all subtypes of malignancies in need of proton therapy.

Conclusion

Patient experiences in this study clearly indicate that oncologists who prepare and follow up patients treated with particle therapy abroad must have sufficient experience of this treatment modality, prognoses, acute side effects, and late complications. We believe that the knowledge derived from this project may lead to better treatment preparation and compliance, enhance understanding of individual patient challenges to reduce stress and worry, and improve follow-up procedures and consequently quality of life of this group of bone sarcoma patients.

Conflicts of Interest

The Authors declare that they have no competing interests in relation to this study.

Authors' Contributions

Ø.S.B. conceived the initial concept and both Ø.S.B and L.F. developed the study design. Ø.S.B. and N.L.J. recruited the patients. L.F. conducted the interviews and analyzed and interpreted the qualitative data. L.F., Ø.S.B., N.L.J and H.B. were all involved in evaluating the findings. All Authors participated in writing the manuscript and have read and agreed to the published version.

Acknowledgements

The Authors are grateful to all the participants for their kind and crucial contributions to this study.

Funding

This study received financial support from the Sissener Foundation (NO 19/11.21).

References

- 1 Winnette R, Hess LM, Nicol SJ, Tai DF and Copley-Merriman C: The patient experience with soft tissue sarcoma: a systematic review of the literature. *Patient* 10(2): 153-162, 2017. PMID: 27744499. DOI: 10.1007/s40271-016-0200-1
- 2 Barrera M, Teall T, Barr R, Silva M and Greenberg M: Health related quality of life in adolescent and young adult survivors of lower extremity bone tumors. *Pediatr Blood Cancer* 58(2): 265-273, 2012. PMID: 21319288. DOI: 10.1002/pbc.23017
- 3 Fauske L, Bruland OS, Grov EK and Bondevik H: Cured of primary bone cancer, but at what cost: a qualitative study of functional impairment and lost opportunities. *Sarcoma* 2015: 484196, 2015. PMID: 25949211. DOI: 10.1155/2015/484196
- 4 Weaver R, O'Connor M, Sobhi S, Carey Smith R and Halkett G: The unmet needs of patients with sarcoma. *Psychooncology* 29(7): 1209-1216, 2020. PMID: 32419264. DOI: 10.1002/pon.5411
- 5 Verma V, Simone CB 2nd and Mishra MV: Quality of life and patient-reported outcomes following proton radiation therapy: a systematic review. *J Natl Cancer Inst* 110(4), 2018. PMID: 29028221. DOI: 10.1093/jnci/djx208
- 6 Srivastava A, Vischioni B, Fiore MR, Vitolo V, Fossati P, Iannalfi A, Tuan JK and Orecchia R: Quality of life in patients with chordomas/chondrosarcomas during treatment with proton beam therapy. *J Radiat Res* 54(Suppl 1): i43-i48, 2013. PMID: 23824125. DOI: 10.1093/jrr/rrt057
- 7 Langegård U, Ahlberg K, Björk-Eriksson T, Fransson P, Johansson B, Ohlsson-Nevo E, Witt-Nyström P and Sjövall K: The art of living with symptoms: a qualitative study among patients with primary brain tumors receiving proton beam therapy. *Cancer Nurs* 43(2): E79-E86, 2020. PMID: 30688666. DOI: 10.1097/NCC.0000000000000692
- 8 Möllerberg ML, Langegård U, Ohlsson-Nevo E, Fransson P, Johansson B, Ahlberg K and Sjövall K: Managing an altered social context-Patients experiences of staying away from home while undergoing proton beam therapy. *Nurs Open* 7(4): 1157-1163, 2020. PMID: 32587735. DOI: 10.1002/nop.2.490
- 9 H-Yazdi N and Meadows R: Child Proton Beam Therapy: A qualitative study of parental views on treatment and information sources. *Radiography (Lond)* 27(1): 101-107, 2021. PMID: 32669230. DOI: 10.1016/j.radi.2020.06.016
- 10 Cockle SG and Ogden J: The 'radiation vacation': Parents' experiences of travelling to have their children's brain tumours treated with proton beam therapy. *Health Psychol Open* 3(1): 2055102916649767, 2016. PMID: 28070403. DOI: 10.1177/2055102916649767
- 11 Olsen DR, Bruland OS, Frykholm G and Norderhaug IN: Proton therapy – a systematic review of clinical effectiveness. *Radiother Oncol* 83(2): 123-132, 2007. PMID: 17499374. DOI: 10.1016/j.radonc.2007.03.001
- 12 Grau C, Durante M, Georg D, Langendijk JA and Weber DC: Particle therapy in Europe. *Mol Oncol* 14(7): 1492-1499, 2020. PMID: 32223048. DOI: 10.1002/1878-0261.12677
- 13 Bortfeld TR and Loeffler JS: Three ways to make proton therapy affordable. *Nature* 549(7673): 451-453, 2017. PMID: 28959981. DOI: 10.1038/549451a
- 14 Tambas M, van der Laan HP, Steenbakkens RJHM, Doyen J, Timmermann B, Orlandi E, Hoyer M, Haustermans K, Georg P, Burnet NG, Gregoire V, Calugaru V, Troost EGC, Hoebbers F, Calvo FA, Widder J, Eberle F, van Vulpen M, Maingon P, Skóra T, Weber DC, Bergfeldt K, Kubes J and Langendijk JA: Current practice in proton therapy delivery in adult cancer patients across Europe. *Radiother Oncol* 167: 7-13, 2022. PMID: 34902370. DOI: 10.1016/j.radonc.2021.12.004
- 15 Chung CS, Yock TI, Nelson K, Xu Y, Keating NL and Tarbell NJ: Incidence of second malignancies among patients treated with proton *versus* photon radiation. *Int J Radiat Oncol Biol Phys* 87(1): 46-52, 2013. PMID: 23778197. DOI: 10.1016/j.ijrobp.2013.04.030
- 16 Uhl M, Herfarth K and Debus J: Comparing the use of protons and carbon ions for treatment. *Cancer J* 20(6): 433-439, 2014. PMID: 25415691. DOI: 10.1097/PPO.0000000000000078
- 17 Lomax AJ: Myths and realities of range uncertainty. *Br J Radiol* 93(1107): 20190582, 2020. PMID: 31778317. DOI: 10.1259/bjr.20190582
- 18 Paganetti H: Relative biological effectiveness (RBE) values for proton beam therapy. Variations as a function of biological endpoint, dose, and linear energy transfer. *Phys Med Biol* 59(22): R419-R472, 2014. PMID: 25361443. DOI: 10.1088/0031-9155/59/22/R419
- 19 Molinelli S, Magro G, Mairani A, Allajbej A, Mirandola A, Chalaszczyk A, Imparato S, Ciocca M, Fiore MR and Orlandi E: How LEM-based RBE and dose-averaged LET affected clinical outcomes of sacral chordoma patients treated with carbon ion radiotherapy. *Radiother Oncol* 163: 209-214, 2021. PMID: 34506829. DOI: 10.1016/j.radonc.2021.08.024
- 20 Thariat J, Hannoun-Levi JM, Sun Myint A, Vuong T and Gérard JP: Past, present, and future of radiotherapy for the benefit of patients. *Nat Rev Clin Oncol* 10(1): 52-60, 2013. PMID: 23183635. DOI: 10.1038/nrclinonc.2012.203
- 21 Baumann BC, Mitra N, Harton JG, Xiao Y, Wojcieszynski AP, Gabriel PE, Zhong H, Geng H, Doucette A, Wei J, O'Dwyer PJ, Bekelman JE and Metz JM: Comparative effectiveness of proton vs photon therapy as part of concurrent chemoradiotherapy for locally advanced cancer. *JAMA Oncol* 6(2): 237-246, 2020. PMID: 31876914. DOI: 10.1001/jamaoncol.2019.4889
- 22 Frisch S and Timmermann B: The evolving role of proton beam therapy for sarcomas. *Clin Oncol (R Coll Radiol)* 29(8): 500-506, 2017. PMID: 28506520. DOI: 10.1016/j.clon.2017.04.034

- 23 Weber DC, Malyapa R, Albertini F, Bolsi A, Kliebsch U, Walser M, Pica A, Combescure C, Lomax AJ and Schneider R: Long term outcomes of patients with skull-base low-grade chondrosarcoma and chordoma patients treated with pencil beam scanning proton therapy. *Radiother Oncol* *120(1)*: 169-174, 2016. PMID: 27247057. DOI: 10.1016/j.radonc.2016.05.011
- 24 Mercado CE, Holtzman AL, Rotondo R, Rutenberg MS and Mendenhall WM: Proton therapy for skull base tumors: A review of clinical outcomes for chordomas and chondrosarcomas. *Head Neck* *41(2)*: 536-541, 2019. PMID: 30537295. DOI: 10.1002/hed.25479
- 25 Mattke M, Vogt K, Bougatf N, Welzel T, Oelmann-Avendano J, Hauswald H, Jensen A, Ellerbrock M, Jäkel O, Haberer T, Herfarth K, Debus J and Uhl M: High control rates of proton- and carbon-ion-beam treatment with intensity-modulated active raster scanning in 101 patients with skull base chondrosarcoma at the Heidelberg Ion Beam Therapy Center. *Cancer* *124(9)*: 2036-2044, 2018. PMID: 29469932. DOI: 10.1002/cncr.31298
- 26 Amichetti M, Amelio D, Cianchetti M, Enrici RM and Minniti G: A systematic review of proton therapy in the treatment of chondrosarcoma of the skull base. *Neurosurg Rev* *33(2)*: 155-165, 2010. PMID: 19921291. DOI: 10.1007/s10143-009-0235-z
- 27 Musha A, Kubo N, Kawamura H, Okano N, Sato H, Okada K, Osu N, Yumisaki H, Adachi A, Takayasu Y, Shino M, Nikkuni O, Ida S, Shirai K, Saitoh JI, Yokoo S, Chikamatsu K and Ohno T: Carbon-ion radiotherapy for inoperable head and neck bone and soft-tissue sarcoma: prospective observational study. *Anticancer Res* *42(3)*: 1439-1446, 2022. PMID: 35220237. DOI: 10.21873/anticancer.15614
- 28 Hameed M and Dorfman H: Primary malignant bone tumors—recent developments. *Semin Diagn Pathol* *28(1)*: 86-101, 2011. PMID: 21675380. DOI: 10.1053/j.semdp.2011.02.002
- 29 Brinkmann S and Kvale S: Interviews: Learning the craft of qualitative research interviewing. 3rd edn. Thousand Oaks, CA, USA, Sage, 2015.
- 30 Edmonds WA and Kennedy TD: An applied guide to research designs: Quantitative, qualitative, and mixed methods. Second edn. Los Angeles, CA, USA, Sage, 2017.
- 31 Gubrium JF, Holstein JA, Marvasti AB and McKinney KD: The sage handbook of interview research: The complexity of the craft. Thousand Oaks, CA, USA, Sage, 2012.
- 32 Braun V and Clarke V: Using thematic analysis in psychology. *Qualitative Research in Psychology* *3(2)*: 77-101, 2017. DOI: 10.1191/1478088706qp063oa
- 33 Braun V and Clarke V: Reflecting on reflexive thematic analysis. *Qualitative Research in Sport, Exercise and Health* *11(4)*: 589-597, 2019. DOI: 10.1080/2159676X.2019.1628806
- 34 Berger AM, Mooney K, Alvarez-Perez A, Breitbart WS, Carpenter KM, Cella D, Cleeland C, Dotan E, Eisenberger MA, Escalante CP, Jacobsen PB, Jankowski C, LeBlanc T, Liguori JA, Loggers ET, Mandrell B, Murphy BA, Palesh O, Pirl WF, Plaxe SC, Riba MB, Rugo HS, Salvador C, Wagner LI, Wagner-Johnston ND, Zachariah FJ, Bergman MA, Smith C and National comprehensive cancer network: Cancer-related fatigue, Version 2.2015. *J Natl Compr Canc Netw* *13(8)*: 1012-1039, 2015. PMID: 26285247. DOI: 10.6004/jnccn.2015.0122
- 35 Fallowfield L, Ford S and Lewis S: No news is not good news: information preferences of patients with cancer. *Psychooncology* *4(3)*: 197-202, 1995. PMID: 11655006. DOI: 10.1002/pon.2960040305
- 36 Baile WF and Aaron J: Patient-physician communication in oncology: past, present, and future. *Curr Opin Oncol* *17(4)*: 331-335, 2005. PMID: 15933462. DOI: 10.1097/01.cco.0000167738.49325.2c
- 37 Beach WA, Easter DW, Good JS and Pigeron E: Disclosing and responding to cancer “fears” during oncology interviews. *Soc Sci Med* *60(4)*: 893-910, 2005. PMID: 15571904. DOI: 10.1016/j.socscimed.2004.06.031
- 38 Shea-Budgell MA, Kostaras X, Myhill KP and Hagen NA: Information needs and sources of information for patients during cancer follow-up. *Curr Oncol* *21(4)*: 165-173, 2014. PMID: 25089098. DOI: 10.3747/co.21.1932
- 39 PTCOG - Facilities in Operation. Available at: <https://www.ptcog.ch/index.php/facilities-in-operation-restricted> [Last accessed on March 7, 2023]
- 40 PTCOG - Facilities under construction. Available at: <https://www.ptcog.ch/index.php/facilities-under-construction> [Last accessed on March 7, 2023]

Received February 27, 2023

Revised March 7, 2023

Accepted March 8, 2023