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ROLE OF INTRAOPERATIVE RADIOTHERAPY IN THE TREATMENT OF SACRAL CHORDOMA

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ABSTRACT

Background context: Sacral chordoma is a rare entity with high local recurrence rates when complete resection is not achieved. Till date, there are not any series available in literature combining surgery and intraoperative radiotherapy (IORT).

Purpose: To report the experience of our Centre in the management of sacral chordoma combining radical resection with both external radiotherapy and intraoperative radiotherapy (IORT).

Study Design: Retrospective case series.

Patients sample: 15 patients with sacral chordoma resected in our centre from 1998 to 2015.

Outcome measures: Overall survival (OS), Disease free survival and rates of local and distant recurrence.

Methods: We retrospectively revised the records of all the patients with sacral chordoma resected in our centre from 1998 to December 2015. Overall survival (OS), Disease free survival and rates of local and distant recurrence were calculated. Results between patients treated with or without IORT were compared.

Results: A total of 15 patients were identified: 8 males and 7 females. Median age was 59 years (range 28-77). IORT was applied in 9 patients and 6 were treated with surgical resection without IORT. In 13 patients we performed the treatment of the primary tumor and in 2 patients we performed the treatment of recurrence disease. A posterior approach was used in 4 patients. Wide surgical margins (R0) were achieved in 6 patients, marginal margins (R1) in 7 patients and there were not any patient with intralesional (R2) margins. At a median follow up of 38 months (range 11-209 months), the 5 years OS in the IORT group was 100% versus 53% in the group of non-IORT *(p=0.05)*. The median DFS in the IORT group was 85 months versus 41 months in the non-IORT group. *I*n the group without IORT, two patients died and nobody died during the follow up in the group treated with IORT. High sacrectomy treated patients had a median survival of 41 months versus 90 months in low sacrectomy treated patients. DFS in patients without gluteal involvement was 100% at 5 years, and 40% in patients with gluteal involvement *(fig 8)*. All patients with a recurrence in our study had gluteal involvement.

Conclusions: Multidisciplinary management of sacral chordoma seems to improve local control. The use of IORT, in our experience, is associated with an increase in overall survival and disease-free survival. The level of resection and gluteal involvement seems to affect survival. The posterior approach is useful in selected cases. Multicenter studies should be performed in order to confirm the utility of IORT.

Keywords: spinal disorders; chordoma; sacral; intraoperative radiotherapy; surgery, sacrectomy

MANUSCRIPT

INTRODUCTION

Chordoma is a rare bone tumor (1-4% of all primary malignant bone tumors), arising from embryonic remnants of the primitive notochord, with a certainly low incidence (<0.1 per 100.000 persons per year)[1-3,7]. The sacrum is the commonest location (40-50%) followed by skull base tumors (35-40%) and vertebral bodies (5-15%)[1-3,7]. Is more common between 5th-7th decades of life and in males. Actually, it's have been reported few cases in ancients and infants, and also in women[4].

They are slow-growing and low grade malignancies, with an insidious clinical presentation[5,6]. They have always been characterized as low metastatic potential, in these cases usually found in lungs[9]. The overall median survival time has been estimated to be approximately 6 years, with a survival rate of 70% at 5 years, falling to 40% at 10 years[9].

Due to the rarity of this disease, randomized studies are unlikely to be performed. Most of studies are retrospective and with low number of patients, so most of them are of low scientific evidence.

Surgery has been so far the cornerstone of treatment[17,18]. Radical surgery is sometimes difficult to achieve (35-75% of R0 margins achieved in different studies) but even when complete resection is obtained there is a high risk of local recurrence[1,8]. When high sacrectomy is required, usually is followed by important morbidity because of S1 and S2 nerve roots injuries that control sexual function, sphincter and mechanical function[10-14].

No conventional chemotherapy has proven any benefit in term of overall survival and local control in patients with chordoma. The advent of molecular targeted therapies has offered some encouraging alternatives for the management of advanced disease[29-31].

In last updated clinic guides, surgery is recommended for treatment of primary and recurrent chordoma, and posteriorly adjuvant radiotherapy[15,16,19,32]. Chordomas have been considered for years as radioresistant tumors[20,21]. Nowadays, and because of better technologies, we can use higher doses of radiotherapy minimizing toxic locorregional activity. Recent advances in radiation in the past 10–15 years for chordomas include conformal photon, proton, and heavy ion therapy with the improving of local control rates and functional outcomes. In numerous studies they report better overall survival (OS) and disease-free survival (DFS) with adjuvant radiotherapy[22-28].

Intraoperative radiotherapy is a modality of radiotherapy in which it is possible to apply the highest dose of radiotherapy with the less possibility of toxic radiation of other structures. This technique allows a theoretical increase in radiation therapeutic index to tumor compared to the adjacent organs at risk for at least three reasons[35]:

The biological effectiveness of a single, high dose of radiation is greater than the same dose administered in fractionated regimen.

The radiation is directed exactly on the area with an increased risk of tumor relapse or persistence.

Irradiation of the dose-limiting organs at risk, such as small intestine, ureters, can be spared from radiation during surgery.

OBJECTIVE AND METHODS

The aim of this study is to report the experience of our Centre in the management of sacral chordoma combining radical resection with intraoperative radiotherapy (IORT).

We retrospectively reviewed our database and analysed all patients with sachral chordoma resected from January 1998 to December 2015. During the analysis of the data we use these variables: age, gender, whether it was a primary chordoma or recurrence, presentation of gluteal involvement, surgical approach (posterior or combined), level of sacrectomy (high or low), tumoral remnants (R0-R2) after surgery, administration of intraoperative radiotherapy (IORT) and/or adjuvant treatment with external radiotherapy, local and systemic recurrences at follow-up, and the time when they appeared, disease-free survival (DFS) time and overall survival (OS) time. All patients are listed in a comprehensive table below *(table 1)*.

There were no patients with evidence of node involvement or distance metastases when surgery was performed. There was no information available about tumor grade in our database.

The surgical procedure consisted in a radical surgery that could be performed by a posterior approach or combining anterior and posterior approach. If we suspected that the tumor had visceral or vascular involvement we always used a combined anterior and posterior approach *(fig 1)*; if not, we tried to use just a posterior approach depending on the sacral level of the lesion, always with the same objective, the complete resection of the tumoral disease.

After resection of the tumor we applied a boost of radiotherapy. The IORT program was performed in a non-dedicated linear accelerator with outpatient radiotherapy activity. Since 2013 we have been using a portable accelerator introduced in the operating room (LIAC 12 MeV by SORDINA). After tumor resection and before reconstruction, a high dose single fraction was delivered to the surgical bed, using high energy electrons beam (*fig 2*). The dose was prescribed to the 90% isodose line, covering the surgical bed and/or directed to the area of concern for a narrow or positive margin of resection. The IORT dose was chosen according to the EBRT dose, margins (intraoperative margin status) and surgical bed volumes. Dose range was 1000-1500 cGys.

Bevelled (15–45 °) lucite circular applicators (size range 5–15 cm) were adjusted to collimate the target surface air gap, allowing dosimetric adaptation and uniform dose distribution.

Finally we performed a soft tissue reconstruction for which we usually carve a TRAM (Transverse Rectus Abdominis Muscle) flap *(fig 3)* or a gluteal flap. When TRAM flap was used for reconstruction, closure of the abdominal wall was done by means of a mesh. The anterior fascia of the rectus abdominis muscle was included in the flap, in order to keep the muscle proportions, but the posterior fascia was left intact at the abdominal wall. The mesh was sutured to the midline and to the border of the oblique muscles. Especial care was taken when suturing the caudal aspect of the mesh to the proximal part of the rectus abdominis muscle. Sutures were placed from the mesh to the anterior fascia, visualizing the vascular pedicle. During this maneuver it was easy to collapse accidently the pedicle if sutures were placed deeply. The rest of the muscle was turned into the pelvis, taking care to avoid any torsion of the pedicle. Later on we placed the flap pullthrough in the posterior part of the pelvis, making a substitution of the bone.

RESULTS:

We analyzed a total of 15 patients (8 men and 7 women) with a sacral chordoma, with a median age of 59 years (range 28-77).

Thirteen patients had primary chordomas and the other two cases had a local recurrence of the disease.

Depending of the vascular or visceral involvement and localization of the tumor, a posterior approach or combining both anterior and posterior approach was used. The posterior approach was performed in nearly one third of our patients (n = 4).

High sacrectomy (S1-S2) was performed in 8 patients and low sacrectomy (S3-S4) in 5 patients.

After surgery, anatomopathological analysis reported resection R0 (zero residue) in 6 patients and a microscopic residue (R1) in 7 patients. There were no patients with macroscopic margins described as positive (R2).

After radical resection of the tumor, 60% of the cases were treated with IORT (n = 9). Regarding the adjuvant treatment, 7 patients (47%) received external beam radiotherapy. Three patients received neoadjuvant radiotherapy because there was evidence of locorregional involvement and wanted to reduce the risk of surgical tumor residue. The other 4 patients recieved adjuvant radiotherapy after surgery.

At a median follow-up of 38 months (range 11-209 months), 6 patients had local recurrence and 2 had a distal recurrence. All with local recurrence after primary surgery were reoperated and they were still alive at the end of the study. Two patients of the study died, one because of distal recurrence and the other one without tumoral evidence.

The 5 year OS of the serie was 83% *(fig 4)*. Regarding DFS in the overall patient serie, we find a median DFS of 85 months, 53% at 5 years and 32% at 10 years *(fig 4)*. When examining the data only in a group of primary chordomas, we found a 5 years OS of 90% and a DFS of 63% at 5 years.

Analyzing survival by stratifying patients into two groups depending on whether they received IORT or not during the intervention, we obtain benefit in 5 years OS *(fig 5)* in the IORT group with 100% versus 53% in the group of non-IORT *(p=0.05)*. The median DFS in the IORT group was 85 months versus 41 months in the non-IORT group. The 5 years DFS rate was 59% in the IORT group and 54% in the non-IORT group *(p=0.75)*.

Considering the residual tumor after resection, both patients with R0 resection and patients with R1 resection had a 5 years OS of 80% *(p=0.85)*. When analyzing DFS we found a median of 85 months in the R0 group, compared to 41 months in the R1 group; and a 5 years DFS rate of 66% in the R0 group versus 40% in the R1 group *(p=0.77)*.

We analyzed the impact of IORT according to the residual tumor, we found similar survival in both R0 and R1 with a 5 years OS in IORT group of 100%. However in the group without IORT, these survival was 50% both in patients with R0 and R1. The 5 years DFS in patients R0 is 75% in the IORT group and 50% in the group without IORT, with a median survival of 85 versus 13 months respectively. In patients R1 the 5 years DFS is 33% in the IORT group versus 50% in the non-IORT group, with a median of 39 versus 41 months respectively.

Comparing the data according to the level of the sacrectomy, we found a 5 year DFS rate of 40% with a median DFS of 41 months in the high-sacrectomy group, compared to a 5 year DFS of 66% and a median DFS of 90 months in the group of low sacrectomy.

Gluteal involvement was present in 7 patients and absent in 3 patients, without having data regarding the rest of patients. DFS in patients without gluteal involvement was 100% at 5 years, and 40% in patients with gluteal involvement. All patients with a recurrence in our study had gluteal involvement.

DISCUSSION

Chordomas are rare primary bone tumors with a high risk for local recurrence and low propensity for distant metastasis. Surgery is the primary modality to achieve the best long-term results. The standard of care in the treatment of sacral chordoma is an en bloc sacrectomy with negative margins. However, the location of these tumors in the pelvic ring makes en bloc resection technically challenging. In our experience, in spite of attempting to perform radical surgery in all cases, this was feasible only in nearly half of our patients, according to what can be seen in literature. Furthermore, the achievement of negative margins often required extended resections, resulting in significant morbidities in relation to the level of sacral amputation. Although our

retrospective analysis could not provide details about quality of life, it is well known that the sacrifice of S2 nerve roots translates into a urinary/fecal dysfunction and sexual disorders, and walking ability is affected if S1 roots are involved. In our experience, some patients with urinary dysfunction can benefit from neurostimulation treatment as described by Cunningham et al[12].

When surgery is performed in primary tumors we achieve better results than in recurrent tumors. For this reason this type of rare and challenging-treating tumors must be managed in high experienced centres of sacropelvic surgery and with a multidisciplinary team. Nonetheless when surgery is performed on recurrent tumors still good results are achieved in terms of local control and overall survival. In our serie all patients who developed a recurrence of their tumor were retreated with radical surgery, and they are still alive for years.

Conventional RT has proven its role; however, high doses required for these radioresistant tumors leads to significant toxicity of surrounding normal tissues and limit its therapeutic value. Newer techniques and charged particle radiotherapy allow for better dose delivery and hence better disease control.

Radiation technology has undergone numerous advancements in the past 10–15 years, allowing for the treatment of tumors while minimizing normal tissue toxicity. Zabel-du Bois et al. report a 1 year local control rate of 79% in 17 sacral chordoma patients treated postoperatively and definitively with Intensity-Modulated RT with a median dose of 54 Gy with significantly improved local control in patients treated >60 Gy[33]. DeLaney et al. reported on 59 patients with spine chordomas, chondrosarcomas, and other sarcomas (including 58% chordomas), treated with surgery and/or photon/proton beam radiation with median follow-up of 7.3 years, 8 year local control was 85% for primary tumors of the spine[23].

The efficacy of IORT for other type of locally advanced tumors has been previously addressed in several studies[35-38]. IORT in our serie had a direct impact on OS independently of the residual status. In our knowledge, this study might be the first one analyzing the effects of IORT administration in patients with sacral chordoma.

Concerning the surgical approach to facilitate adequate tumor resection, most authors preferred a combined anterior and posterior approach to provide an adequate approach to the tumor. Although the anterior approach is strongly recommended for high sacral chordoma tumors, the posterior approach is adequate for total resection for low sacral resection and when the rectum is not involved because it is a safer and easier procedure to do, with a lower risk of abdominal complications.

In our experience gluteal infiltration, had a direct impact on DFS and local recurrence. Yonemoto et al. mentioned that it is highly possible that residual chordoma infiltrating the gluteal muscles accounts for the local recurrences[34]. A precise preoperative assessment of the tumor infiltration into the gluteal muscles by MRI is important for the adequate design of the surgical intervention.

The surgical literature comprised retrospective reviews of low and very low quality evidence. These studies include a heterogeneous mix of patients, with primary and recurrent disease, treated with similarly varied treatment regimens that typically including surgery and/or RT. Nevertheless, given the poor rates of local control with surgery alone, and the suggestion of improved local control in RT studies, it seems reasonable to offer adjuvant RT in these patients[39].

This study has some important limitations because of retrospective data and small number of patients. Furthermore the degrees of the tumor resection could be different by using different approaches, so the approaches could indirectly affect the prognosis and outcomes. Although there were no patients with evidence of node involvement or distance metastases when surgery was performed, there was no information available about tumor size and grade in our database. These are important prognostic factors so there is a concern for accuracy of the conclusion. However, this study reports a serie of consecutive patients with sacral chordoma, providing a reasonable median follow-up. In very rare cancers, retrospective series or multicentric studies may be the only opportunity to understand the natural history of the disease. This applies to chordoma.

limitiations of the study are small numbers (only 9 in the treated group), mixed followup with some only 2-3 year f/u and with various surgical approaches.

CONCLUSIONS:

In conclusion the treatment of sacral chordoma in a center with high experience in sacropelvic tumors seems to improve the local control of the disease. The level of resection, gluteal involvement and relapse are factors of poor prognosis. The use of IORT in our experience is associated with an increase in overall survival and disease-free survival. Other studies should be done to confirm these benefits of IORT.

REFERENCES

Aylon T, Torabi R, et al. Management of Locally Recurrent Chordoma of the Mobile Spine and Sacrum. *Spine* 2016;Vol41: Number 20S, pp S193-S198.

Ropper AE, Cahill KS, Hanna JW, et al. Primary vertebral tumors: a review of epidemiologic, histological and imaging findings, part II: locally aggressive and malignant tumors. Neurosurgery 2012;70:211 – 9.

Sciubba DM, Chi JH, Rhines LD, et al. Chordoma of the spinal column. Neurosurg Clin N Am 2008;19:5 – 15.

Garofalo F, Di Summa PG, et al. Multidisciplinary Approach of Lumbo-Sacral Chordoma: From Ongological Treatment to Reconstructive Surgery. *Journal of Surgical Oncology* 2015;112:544-554.

Depsey P, Morris S, et al. Sacral epidural Chordoma. *The Spine Journal* 2016. Images of Spine Care.

Ferraresi V, Nuzzo C, et al. Chordoma: clinical characteristics, management and prognosis of a case series of 25 patients. *BMC Cancer* 2010, 10:22.

Zou MX, Lv GH, et al. Tumor size as a Prognostic Factor in Spinal Chordoma: A Systematic Literature Review. *Spine* 2016 [Epub ahead of print].

Radaelli S, Stacchiotti S, et al. Sacral Chordoma: Long-term Outcome of a Large Series of Patients Surgically Treated at Two Reference Centers. *Spine* 2016;Vol41: Number 12, pp 1049-1057.

Chugh R, Tawbi H, et al. Chordoma: The Nonsarcoma Primary Bone Tumor. *The Oncologist* 2007, 12:1344-1350.

Schwab JH. What are the Conditional Survival and Functional Outcomes After Surgical Treatment of 115 Patients with Sacral Chordoma? *Clin Orthp Relat Res* 2016. doi 10.1007/s1999-016-4871-7,

Fabbri N. How Does the Level of Nerve Root Resection in En Bloc Sacrectomy Influence Patient-Reported Outcomes? *Clin Orthp Relat Res* 2016. doi 10.1007/s1999-016-4897-x

Cunningham KG, Westney OL. Sacral Neuromodulation for the Treatment of Retention in Partial Sacrectomy Patients. *Neuromodulation* 2016. doi 10.1111/ner.12455.

Sabuncuoglu H, Ozdogan S, et al. Total Resection of Inferiorly Located Sacral Chordoma with Posterior Only Approach: Case Report and Review of the Literature. *Turkish Neurosurgery* 2010, Vol20, No4, 527-532.

Asavamongkolkul A, Waikakul S. Wide resection of sacral chordoma via a posterior approach. *International Orthopaedics* 2012. 36:607-612.

Walcott BP, Nahed BV, et al. Chordoma: current concepts, management, and future directions. *Lancet Oncol* 2012; 13:e69-76,

Chen K, Yang H, et al. Review of current treatment of sacral chordoma. *Orthopaedic Surgery* 2009. Vol 1. No3, 238-244.

García-Sabrido JL, Vega D, et al. Tumores sacropélvicos primarios y secundarios. Tratamiento con cirugía radical y radioterapia intraoperatoria. *Cir Esp* 2003;73(2):78-87.

Ruggieri P, Angelini A, et al. Surgical Margins and Local Control in Resection of Sacral Chordomas. *Clin Orthop Relat Res* 2010;468:2939-2947.

Ailon T, Torabi R, et al. Management of Locally Recurrent Chordoma of the Mobile Spine and Sacrum: A Systematic Review. *Spine* 2016;41(20):S193-S198.

Yu E, Koffer PP, et al. Incidence, Treatment, and Survival Patterns for Sacral Chordoma in the United States, 1974-2011. *Frontiers in Oncology* 2016. doi: 10.3389/fonc.2016.00203.

Fourney DR, Gokaslan ZL. Current management of sacral chordoma. *Neurosurg Focus* 2003. 15(2):Article 9.

Pennicooke B, Laufer I, et al. Safety and Local Control of Radiation Therapy for Chordoma of the Spine and Sacrum. *Spine* 2016;Vol41: Number 20S, pp S186-S192.

F. Delaney TF, Liebsch, et al. Long-Term Results of Phase II Study of High Dose Photon/Proton Radiotherapy in the Management of Spine Chordomas, Chodrosarcomas, and Other Sarcomas. *Journal of Surgical Oncology* 2014; 110:115-122

Riopel C, Michot C. Les chordomes. *Ann Pathol* 2007; 27:6-15.

Rotondo RL, Szymonifka J, et al. High-dose Proton-beam Based Radiation Therapy (RT) with or without Surgery in the Management of Primary and Recurrent Spine Chordomas (CH): A retrospective Review of Outcomes and Clinicopathologic Prognostic Factors. *Radiation Oncology* 2011; Vol81, number2.

Imai R, Kamada T, et al. Carbon ion radiotherapy for sacral chordoma. *The British Journal of Radiology* 2011;84:S48-S53.

Pennicooke B, Laufer I, et al. Safety and Local Control of Radiation Therapy for Chordoma of the Spine and Sacrum: A Systematic Review. *Spine* 2016;41(20):S186-S192.

Lorenzo C, Andrea P, et al. Surgical spacer placement prior carbon ion radiotherapy (CIRT): an effective feasible strategy to improve the treatment for sacral chordoma. *World J Surg Oncol* 2016;14(1):211.

Launay SG, Chetaille B, et al. Efficacy of epidermal growth factor receptor targeting in advanced chordoma: case report and literature review. *BMC Cancer* 2011, 11:423.

Tamborini E, Virdis E, et al. Analysis of receptor tyrosine kinases (RTKs) and downstream pathways in chordomas. *Neuro-Oncology* 2010; 12(8):776-789.

Casali PG, Messina A, et al. Imatinib Mesylate in Chordoma. *Cancer* 2004. Vol 101, Number 9.

Stacchiotti S, Sommer J. Chordoma Global Consensus Group. Building a global consensus approach to chordoma: a position paper from the medical and patient community. Lancet Oncol 2015;16:e71 – 83.

Zabel-du Bois A, Nikoghosyan A, Schwahofer A, Huber P, Schlegel W, Debus J, et al. Intensity modulated radiotherapy in the management of sacral chordoma in primary versus recurrent disease. *Radiother Oncol* (2010) 97(3):408–12. doi:10.1016/j.radonc.2010.10.008

Yonemoto T, Tatezaki S, Takenouchi T, Ishii T, Satoh T, Moriya H: The surgical management of sacrococcygeal chordoma. Cancer 88(9):2122-2134, 1999

Valentini V, Calvo F, et al. Intraoperative radiotherapy (IORT) in pancreatic cancer: joint analysis of the ISIORT-Europe experience. *Radiotherapy and Oncology 2009*. 91:54-59.

Calvo FA, Sole CV, Atahualpa F, et al. Chemoradiation for resected pancreatic adenocarcinoma with or without intraoperative radiation therapy boost: Long-term outcomes. *Pancreatology 2013*. 13; 576-582.

Calvo FA, Sole CV, Obregón R, et al. Intraoperative radiotherapy for the treatment of resectable locally advanced gastric adenocarcinoma: topography of locoregional recurrences and long-term outcomes. *Clin Transl Oncol 2013*. 14:443-449.

Yu W, Guo Y, Zhang Q, Fu S. Benefits from adjuvant intraoperative radiotherapy treatment for gastric cancer: a meta-analysis. *Molecular and Clinical Oncology 2015*. 3:185-189.

Stacchiotti S, Gronchi A, et al. Best practices for the Management of Local-regional Recurrent Chordoma. A Position Paper by the Chordoma Global Consensus Group. *Ann Oncol 2017*. doi: 10.1093/annonc/mdx054

Figure 1. Left image: Anterior approach, iliac vessels are disected and tumor is exposed. Right image: Posterior approach, tumor is resected and sacrectomy has been performed.

Figure 2. Accelerator for IORT. Organs of risk are protected.

Figure 3. TRAM flap.

Figure 4. Overall Survival (left image) and Disease-Free Survival (right image) of the hole population of the study.

Figure 5. Overall Survival (left image) and Disease-Free Survival (right image) of patients with or without IORT.

Table 1. All patients of the study listed.

Patient	Gender	Age	Primary tumor or Recurrence	Treatment	Residual tumor	Follow up (months)	Recurrence	Final out-come
Patient # 1	Male	28	Recurrence	Surgery + RT	R0	13	Yes	Not Alive
Patient # 2	Female	77	Primary tumor	Surgery + IORT	R0	92	Yes	Alive
Patient # 3	Female	59	Primary tumor	Surgery + IORT	R0	180	Yes	Alive
Patient # 4	Male	39	Primary tumor	Surgery + IORT	R1	38	No	Alive
Patient # 5	Female	43	Primary tumor	Surgery + IORT	N/A	204	No	Alive
Patient # 6	Male	70	Primary tumor	Surgery + IORT	R1	91	Yes	Alive
Patient # 7	Female	48	Primary tumor	Surgery + IORT + RT	R0	131	No	Alive
Patient # 8	Male	61	Recurrence	Surgery + IORT + RT	R1	12	No	Alive
Patient # 9	Female	57	Primary tumor	Surgery	R1	11	Yes	Alive
Patient # 10	Male	56	Primary tumor	Surgery + IORT + RT	R1	30	Yes	Alive
Patient # 11	Male	49	Primary tumor	Surgery	R1	56	No	Alive
Patient # 12	Female	71	Primary tumor	Surgery + RT	R1	30	No	Not Alive
Patient # 13	Female	60	Primary tumor	Surgery + IORT + RT	R0	11	No	Alive
Patient # 14	Male	68	Primary tumor	Surgery	R0	16	Yes	Alive
Patient # 15	Male	64	Primary tumor	Surgery + RT	N/A	209	Yes	Alive

N/A: Non available, R0: Non surgical residue, R1: Microscopic residue, IORT: IntraOperative RadioTherapy, RT: RadioTherapy.