New Perspectives and State of the Art in Interventional Radiotherapy (Brachytherapy) for Head and Neck Tumors

MARIA CONCETTA LA MILIA[1], ENRICO ROSA[2,3], PIERPAOLO DRAGONETTI[1,2], BRUNO FIONDA[2], ELISA PLACIDI[2], VALENTINA LANCELLOTTA[2], MARTINA DE ANGELI[2], FRANCESCO PASTORE[2], MARIANGELA MASSACCESI[2], FRANCESCO MICCICHÈ[4], LEONARDO BANNONI[2], JACOPO GALLI[1,2], MARCO DE SPIRITO[1,2], MARIA ANTONIETTA GAMBACORTA[1,2], FRANCESCO BUSSU*[5,6], LUCA TAGLIAFERRI*[1,2]
*Equal contribution as last author

[1]Università Cattolica del Sacro Cuore, [2]Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, [3]eCampus University, Novedrate, [4]Ospedale Isola Tiberina–Gemelli Isola, Rome, [5]Azienda Ospedaliero Universitaria Sassari, [6]University of Sassari, Sassari, Italy

Levelezési cím:
Enrico Rosa, UOC Fisica per le Scienze Della Vita, Fondazione Policlinico Universitario A. Gemelli IRCCS, Largo A. Gemelli 8, Rome, 00168, Italy. E-mail: enrico.rosa@guest.policlinicogemelli.it

Közlésre érkezett:
2025. január. 14.
Elfogadva:
2025. február. 10.

Aim: *This review aims to evaluate the role of interventional radiotherapy (IRT – brachytherapy) in the clinical management of head and neck (H&N) cancers, focusing on recent technological advancements and their impact on clinical outcomes.*
Methods: *A comprehensive literature review of clinical applications of IRT in H&N cancers was conducted, emphasizing the role of advanced imaging intensity-modulated IRT and custom applicators. The role of artificial intelligence and several dose calculation algorithms in treatment planning was also analyzed.*
Results: *IRT demonstrated efficacy across primary treatment, postoperative settings, and reirradiation, offering precise dose delivery while sparing adjacent healthy tissues. Innovations such as image-guided techniques and personalized 3D-printed applicators improved dosimetric accuracy and reduced toxicity. Functional outcomes were particularly favorable in sensitive anatomical regions like the nasal vestibule and oral cavity.*
Conclusions: *IRT remains a cornerstone of precision oncology for head and neck cancers, achieving high efficacy, reduced toxicity, and improved patient quality of life. These advancements highlight its crucial role in modern oncologic care. Magy Onkol 69:143-147, 2025*

Keywords: *interventional radiotherapy, brachytherapy, head and neck tumors, clinical practice, dosimetry*

Cél: Közleményünk célja az intervenciós radioterápia (IRT – brahiterápia) szerepének értékelése a fej-nyaki (H&N) daganatok kezelésében, a legújabb technológiai fejlesztésekre és azoknak a klinikai eredményekre gyakorolt hatására összpontosítva.
Módszerek: Átfogó irodalmi áttekintés az IRT klinikai alkalmazásáról a H&N daganatos megbetegedésekben, hangsúlyozva a fejlett képalkotó intenzitásmodulált IRT és az egyedi applikátorok szerepét. A mesterséges intelligencia és dózisszámítási algoritmusok szerepének elemzése a kezelés tervezésében.
Eredmények: Az IRT hatékonynak bizonyult az elsődleges kezelés, a posztoperatív ellátás és a reirradiáció során, pontos dózisleadást biztosítva a szomszédos egészséges szövetek kímélete mellett. Az olyan innovációk, mint a képvezérelt technikák és a személyre szabott 3D-nyomtatott applikátorok javították a dozimetriai pontosságot és csökkentették a toxicitást.
Következtetések: Az IRT továbbra is a precíziós onkológia sarokköve marad a fej-nyaki rákok esetében, magas hatékonyságot, csökkentett toxicitást és jobb életminőséget biztosítva.

La Milia MC, Rosa E, Dragonetti P, Fionda B, Placidi E, Lancellotta V, De Angeli M, Pastore F, Massaccesi M, Miccichè F, Bannoni L, Galli J, De Spirito M, Gambacorta MA, Bussu F, Tagliaferri L. A fej-nyaki daganatok intervenciós sugárterápiájának (brahiterápia) korszerű technikái és új perspektívái Magy Onkol 69:143-147, 2025

Kulcsszavak: intervenciós sugárkezelés, brahiterápia, fej-nyaki tumorok, klinikai gyakorlat, dozimetria

INTRODUCTION

Head and neck cancers include a wide range of malignancies that are challenging to treat due to their complex anatomy and proximity to critical structures. Interventional radiotherapy (IRT – brachytherapy) offers a highly targeted radiation treatment by placing radioactive sources directly within or near the tumor. This technique has greatly benefited from advancements in imaging, dosimetry, and catheter design, which have improved its effectiveness while reducing side effects (1).

IRT has been successfully applied in various clinical scenarios (tumor histologies, primary sites, treatment targets, different disease phases for exclusive, adjuvant and palliative purposes) and implant types. It has shown efficacy in managing both primary and recurrent head and neck tumors (2). Specifically, postoperative IRT can be considered in patients with close or positive surgical margins, perineural invasion, and lymphovascular invasion, where it enhances local control by delivering a high-dose radiation boost to residual microscopic disease (3).

Its ability to deliver high radiation doses directly to the tumor ensures superior local control rates, while the steep dose fall-off minimizes exposure to nearby organs at risk (OARs), outperforming external beam radiotherapy in this regard (3). In the head and neck region, IRT has been used to treat tumors in locations such as the oral cavity, oropharynx, nasopharynx, nasal vestibule, and paranasal sinuses. Additionally, it has been employed for reirradiation and as a perioperative treatment in combination with surgery, requiring close collaboration among multidisciplinary teams.

Technological advancements include remote after-loading systems, advanced treatment planning software, and image-guided techniques (4). These innovations have enhanced the precision of catheter placement, improved dose distribution, and ensured safety for medical personnel, resulting in better clinical outcomes. Biological planning, which optimizes treatment based on biological parameters rather than solely physical criteria, represents another significant leap forward.

Modern image-guided IRT has revolutionized clinical practice by enabling precise target delineation and sparing critical structures. Techniques such as 3D catheter reconstruction and advanced imaging modalities like CT, MRI, and ultrasound have further refined treatment precision (5). Intensity-modulated IRT (IM-IRT), which combines brachytherapy's precision with the dose conformity of intensity-modulated radiation therapy (IMRT), achieves highly targeted dose delivery while protecting surrounding tissues.

Endoscopy-guided approaches have proven particularly valuable for complex cases, such as sinonasal and nasopharyngeal recurrences, where accurate catheter placement is critical. Custom-made applicators, often produced using 3D printing, enhance the delivery of radiation directly to the tumor while minimizing damage to adjacent tissues (6).

Alongside these innovations, advances in dosimetry, including 3D dose calculations, automated biological dose optimization, and progress in dose calculation algorithms, have significantly improved the accuracy of dose distribution. The integration of artificial intelligence (AI) and custom applicators further refines treatment precision by optimizing both the calculation and delivery of radiation, reducing treatment-related toxicities such as xerostomia, dysphagia, and optic neuropathy (7).

The success of IRT relies heavily on a multidisciplinary approach that integrates the expertise of radiation oncologists, surgeons, radiologists, and medical physicists. Anesthetists also play a critical role in ensuring patient comfort and safety during complex procedures. Depending on the complexity of the interventional radiotherapy procedure, the contribution of each specialist becomes essential to maximize treatment effectiveness (8). Multidisciplinary tumor boards have been shown to significantly enhance personalized treatment strategies, allowing each professional to provide their unique expertise in planning and execution, ultimately leading to improved patient outcomes (9).

METHODS

A review of clinical applications of IRT in head and neck cancers was conducted, emphasizing advanced imaging, intensity-modulated brachytherapy, clinical and dosimetric aspects. To evaluate the state-of-the-art in IRT, all articles presenting advancements in technique or technology were analyzed, focusing on innovations that enhance precision, safety, and clinical efficacy. Particular attention was given to studies addressing improvements in multidisciplinary treatment approaches, including radiation oncology, surgery, and medical physics, as well as the use of AI and model-based dose calculation algorithms in treatment planning. Furthermore, the review incorporated aspects of psychological care and patient-centered treatment strategies, highlighting the importance of electronic symptom monitoring, counseling, and stress management programs in improving patient outcomes. This comprehensive approach aimed to identify developments that contribute to optimizing IRT as a holistic and personalized treatment modality.

RESULTS

Applications in Dosimetry

AI is increasingly recognized as a transformative tool in IRT, particularly in head and neck brachytherapy. AI algorithms, including machine learning and deep learning, have demonstrated significant potential in automating key processes such as target delineation, treatment planning, and dose optimization (10). Neural networks trained on extensive datasets can accurately identify optimal catheter placements and predict radiation dose distributions with remarkable precision, substantially reducing planning times. Additionally, AI-powered predictive models analyze clinical, imaging, and dosimetric parameters to assist clinicians in selecting the most suitable patients for treatment, ensuring the development of personalized treatment plans. The integration of AI into real-time quality assurance systems enhances safety by identifying deviations from planned treatment protocols during procedures, enabling immediate corrective actions (11).

In head and neck IRT, ongoing research focuses on improving dose calculation algorithms to overcome the limitations of the TG-43 protocol (12), a standardized dosimetry formalism for IRT developed by the American Association of Physicists in Medicine, which calculates dose distribution based on source geometry, activity, and medium properties, assuming a homogeneous water medium for dose calculations. Although TG-43 remains the only clinically approved algorithm, it often overestimates doses to OARs compared to model-based dose calculation algorithms (MBDCAs) (13, 14). Studies indicate that TG-43 tends to deliver higher dose estimates for target volumes and critical OARs, such as the skin and ipsilateral lung. This overestimation becomes particularly problematic in scenarios involving tissue interfaces or materials with densities significantly different from water.

Despite its limitations, TG-43 remains central to clinical practice due to its widespread acceptance and standardization. However, advancements in MBDCAs, which incorporate computed tomography (CT)-based calculations and account for tissue heterogeneities and interfaces, promise greater dosimetric precision. Transitioning to these advanced algorithms could enhance treatment safety and efficacy by minimizing unnecessary exposure to OARs while maintaining robust tumor control (15). As research progresses, these more accurate dose calculation methods may redefine clinical standards, enabling optimized outcomes for patients undergoing IRT.

IRT is increasingly being integrated into personalized treatment approaches through advanced imaging and dosimetry. This integration facilitates precise target volume delineation and improves the evaluation of doses delivered to OARs, including sensitive structures such as the eyes, eye lenses, and mandible. These advancements have significantly reduced toxicity while maintaining effective tumor control (16). Additionally, advanced dosimetric studies focusing on protecting OARs have paved the way for safer and more effective treatments. By optimizing dose distribution and minimizing radiation exposure to critical structures, these innovations enhance the therapeutic ratio and improve the quality of life for patients (17). Personalized treatment planning, supported by high-resolution imaging and detailed dosimetric analysis, ensures that each patient's unique anatomy and clinical condition are thoroughly considered. This level of customization balances tumor control with the preservation of function and the reduction of long-term side effects, aligning with the goals of modern radiotherapy.

Technological advancements, particularly in 3D printing, have further enhanced the personalization and effectiveness of IRT. 3D printing has revolutionized the production of patient-specific devices and treatment tools, such as custom-made applicators, boluses, and spacers. These devices are tailored to the patient's unique anatomy, enabling precise dose delivery while minimizing exposure to healthy tissues. Notably, 3D printing has facilitated the creation of personalized guides for catheters used in interstitial brachytherapy, ensuring accurate placement and adaptation to individual anatomical variations (18). Accurate seed placement, guided by CT-based preplanning, is crucial for effective conformal radiotherapy and for minimizing adverse side effects on adjacent normal tissues (19). CT-based preplanning allows for the design and production of personalized applicators or supportive devices that enhance the precision of catheter or seed placement. These tools optimize radiation dose delivery to the target while sparing healthy tissues, resulting in more conformal treatments with reduced risks of side effects.

By combining CT-based preplanning with 3D-printed support structures, clinicians can deliver safer and more effective treatments, improving the accuracy and reproducibility of procedures. Moreover, 3D printing enables rapid prototyping and the creation of complex structures that were previously unobtainable using traditional manufacturing methods. These innovations are transforming IRT, providing clinicians with advanced tools to optimize treatment while aligning with the principles of precision medicine. This integration of cutting-edge technology reinforces the trend toward highly personalized oncologic care, ensuring improved outcomes for patients.

Clinical Practice

IRT's clinical applications in head and neck malignancies include its use as an exclusive treatment for local control of specific tumors and as a complementary modality to external beam radiotherapy. There are different scenarios in which the use of IRT could be useful:

1. IRT alone;
2. IRT boost for dose escalation;
3. postoperative IRT;
4. re-irradiation (IRT alone, or postoperative IRT).

In early-stage disease IRT is considered radical with curative intent. IRT can also be considered as a perioperative technique together with surgery (20). Perioperative IRT (POIRT) consists in tumor resection or debulking and catheter implantation during the same surgery and radiation dose delivery within the perioperative period. POIRT allows effective coverage of target volumes, sparing doses to surrounding normal tissues and offers radiobiological advantages by limiting treatment delay (21). In the adjuvant setting, postoperative IRT may be considered in case of close or positive margins or lymphovascular invasion (22). In cases of recurrences after previous radical treatment re-irradiation can be considered as salvage option, using IRT in combination with external beam radiotherapy (EBRT) or alone as reported

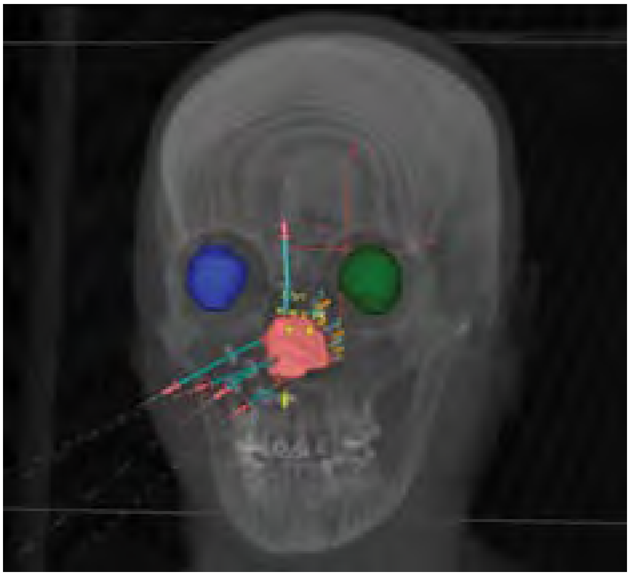

FIGURE 1. Example of reconstruction and treatment planning for a nasal vestibule tumor using an interventional radiotherapy planning system. The highlighted contours delineate the OARs and the lesion considered during the planning process.

by the Groupe Européen de Curiethérapie – European Society for Radiotherapy and Oncology (GEC-ESTRO) recommendations for head & neck cancer IRT (23).

In scenarios such as nasal vestibule *(Figure 1)* and lip tumors *(Figure 2),* IRT ensures excellent aesthetic and functional outcomes while providing targeted dose escalation. Recently, the Oncological Committee of the Italian Society of Otorhinolaryngology defined exclusive IRT as the preferred treatment for primary lesions in nasal vestibule squamous cell carcinomas without bone involvement, while surgery remains the gold standard for the management of the neck nodal spread. In fact, at the level of primary lesion, as for oncological outcomes IRT appears equivalent to surgery but offers clear advantages in terms of anatomic preservation and cosmetic results (24).

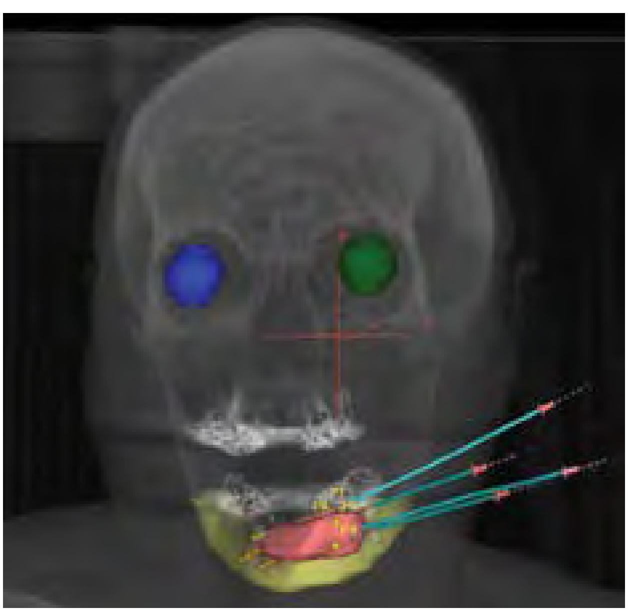

FIGURE 2. Representation of reconstruction and treatment planning for a lip tumor using an interventional radiotherapy planning system. The contours illustrate the OARs and the tumor volume considered during the treatment planning process.

In selected clinical situations, high dose rate (HDR) IRT could be combined with EBRT, showing promising results with acceptable toxicity profiles. HDR-IRT enables the delivery of higher radiation doses directly to the tumor, potentially enhancing local control and reducing the necessity for extensive surgical interventions, such as in the case of tongue tumors. In fact, EBRT allows a uniform dose distribution to larger treatment volumes, reserving HDR-IRT for the final part of the treatment as boost thus decreasing the likelihood of late-onset radiation-induced toxicities (25).

For the nasopharynx, paranasal sinus and nasal vestibule, IRT has the further advantage of maintaining the mucosal functions (including mucociliary clearance and olphaction). In oral cavity cancers, the role of IRT in preserving oral competence, tongue mobility, speech, swallowing and the hard palate has been demonstrated. IRT in oropharyngeal cancers has been shown to reduce xerostomia and dysphagia (26, 27).

Psychological and Adjuvant Support

Psychological interventions and electronic symptom monitoring have been shown to improve survival and patient-reported outcomes, suggesting the importance of integrating patient-centered care into oncology treatments (28). Psychological care, including counseling and stress management programs, has demonstrated benefits in reducing anxiety and depression, improving treatment adherence, and enhancing overall quality of life for cancer patients (29). In parallel, electronic symptom monitoring tools, such as patient-reported outcome systems, enable real-time tracking of treatment-related side effects, facilitating earlier interventions and personalized adjustments to therapy plans. These systems have not only improved communication between patients and healthcare providers but have also been associated with prolonged survival rates by ensuring timely management of complications and maintaining the continuity of care (30, 31). Together, these approaches underscore the value of addressing the psychological and physical needs of patients, paving the way for a more holistic and effective cancer care strategy.

CONCLUSION

IRT has established itself as a highly effective treatment for head and neck cancers, offering precise dose delivery while sparing critical structures. Advances in imaging, catheter technology, and dosimetry, alongside innovations such as

AI and 3D printing, have significantly improved treatment accuracy, safety, and personalization.

IRT's versatility allows its application in various scenarios, including primary treatment, reirradiation, and perioperative techniques, achieving excellent functional and aesthetic outcomes. Multidisciplinary collaboration and patient-centered approaches, including psychological support and symptom monitoring, further enhance its impact on patient care and quality of life.

These advancements solidify IRT as a cornerstone of precision oncology, delivering optimized outcomes even in anatomically complex and challenging cases.

REFERENCES

1. Kirthi Koushik AS, Alva RC: Brachytherapy in head and neck cancers: "Are we doing it or are we done with it". Indian J Surg Oncol 9:171-174, 2018
2. Bussu F, Tagliaferri L, Mattiucci G, et al: HDR interventional radiotherapy (brachytherapy) in the treatment of primary and recurrent head and neck malignancies. Head Neck 41:1667-1675, 2019
3. Margalit DN, Sacco AG, Cooper JS, et al: Systematic review of postoperative therapy for resected squamous cell carcinoma of the head and neck: Executive summary of the American Radium Society appropriate use criteria. Head Neck 43:367-391, 2021
4. Kovács G: Modern head and neck brachytherapy: from radium towards intensity modulated interventional brachytherapy. J Contemp Brachytherapy 6:404-416, 2015
5. Tagliaferri L, Fionda B, Bacorro W, Kovács G: Advances in head-and-neck interventional radiotherapy (brachytherapy). J Med Univ Santo Tomas 8:1338-1341, 2024
6. Lancellotta V, Pagano S, Tagliaferri L, et al: Individual 3-dimensional printed mold for treating hard palate carcinoma with brachytherapy: A clinical report. J Prosthet Dent 121:690-693, 2019
7. Tagliaferri L, Bussu F, Rigante M, et al: Endoscopy-guided brachytherapy for sinonasal and nasopharyngeal recurrences. Brachytherapy 14:419-425, 2015
8. Laskar S, Pilar A, Khanna N, et al: Interstitial brachytherapy for orbital soft tissue sarcoma: an innovative technique. J Contemp Brachytherapy 5:466-471, 2017
9. Fionda B, Placidi E, Lancellotta V, et al: COMIRI – COMplexity Index of interventional Radiotherapy (brachytherapy) Implants: assessment of procedures based on type, equipment, and team. J Contemp Brachytherapy 16:306-309, 2024
10. Iezzi R: Can a dedicated multidisciplinary tumor board improve personalized medicine for patients in interventional oncology? A large retrospective single-center experience. TJ Oncol, 2022. http://onkder.org/pdf/pdf_TOD_1313.pdf
11. Fionda B, Boldrini L, D'Aviero A, et al: Artificial intelligence (AI) and interventional radiotherapy (brachytherapy): state of art and future perspectives. J Contemp Brachytherapy 12:497-500, 2020
12. Fionda B, Placidi E, De Ridder M, et al: Artificial intelligence in interventional radiotherapy (brachytherapy): Enhancing patient-centered care and addressing patients' needs. Clin Transl Radiat Oncol 49:100865, 2024
13. Nath R, Anderson LL, Luxton G, et al: Dosimetry of interstitial brachytherapy sources: Recommendations of the AAPM Radiation Therapy Committee Task Group No. 43. Med Phys 22:209-234, 1995
14. Beaulieu L, Carlsson Tedgren Å, Carrier J, et al: Report of the Task Group 186 on model–based dose calculation methods in brachytherapy beyond the TG–43 formalism: Current status and recommendations for clinical implementation. Med Phys 39:6208-6236, 2012
15. Roussakis Y, Antorkas G, Georgiou L, et al: Dosimetric comparison of AcurosTM BV and AAPM TG-43 formalism for interstitial iridium-192 high-dose-rate brachytherapy. J Contemp Brachytherapy 16:211-218, 2024
16. Placidi E, Fionda B, Rosa E, et al: Dosimetric impact of applying a model-based dose calculation algorithm for skin cancer brachytherapy (interventional radiotherapy). J Contemp Brachytherapy 15:448-452, 2023
17. Fionda B, Bussu F, Placidi E, et al: Interventional radiotherapy (brachytherapy) for nasal vestibule: novel strategies to prevent side effects. J Clin Med 12:6154, 2023
18. Tagliaferri L, Sciurti E, Fionda B, et al: PRO-NOVELTY: Patient-Reported Outcomes in NOse VEstibule interventionaL radioTherapY (brachytherapy). J Clin Med 13:4683, 2024
19. Choi CH, Kim J, Park JM: A 3D-printed patient-specific applicator guide for use in high-dose-rate interstitial brachytherapy for tongue cancer: a phantom study. Phys Med Biol 64:135002, 2019
20. Huang MW, Zhang JG, Zheng L, et al: Accuracy evaluation of a 3D-printed individual template for needle guidance in head and neck brachytherapy. J Radiat Res 57:662-667, 2016
21. Budrukkar A, Guinot JL, Tagliaferri L, et al: Function preservation in head and neck cancers. Clin Oncol 35:497-506, 2023
22. Bacorro W, Fionda B, Soror T, et al: Local control, survival, and toxicity outcomes with high-dose-rate peri-operative interventional radiotherapy (brachytherapy) in head and neck cancers: a systematic review. J Pers Med 14:853, 2024
23. Bhalavat R, Budrukkar A, Laskar SG, et al: Brachytherapy in head and neck malignancies: Indian Brachytherapy Society (IBS) recommendations and guidelines. J Contemp Brachytherapy 12:501-511, 2020
24. Guinot JL, Bacorro W, Budrukkar A, et al: GEC-ESTRO recommendations for head & neck cancer brachytherapy (interventional radiotherapy): 2nd update with focus on HDR and PDR. Radiother Oncol 201:110533, 2024
25. Bussu F, Tagliaferri L, Corbisiero MF, et al: Management of nasal vestibule carcinomas: recommendations by the Oncological Committee of the Italian Society of Otorhinolaryngology – Head and Neck Surgery. Acta Otorhinolaryngol Ital 44:13-20, 2024
26. Murakami N, Sakuramachi M, Kashihara T, et al: The combination of volumetric arc radiation therapy and boost high-dose rate interstitial brachytherapy for T3N2c tongue cancer: a technical report. Jpn J Clin Oncol 53:85-90, 2023
27. Bussu F, Tagliaferri L, De Corso E, et al: Functional results of exclusive interventional radiotherapy (brachytherapy) in the treatment of nasal vestibule carcinomas. Brachytherapy 20:178-184, 2021
28. Galli J, Bussu F, Passali GC, et al: Brachytherapy for nose vestibule malignancies: functional results. In: Malignancies of the Nasal Vestibule. Ed. Bussu F, Cham, Springer International Publishing, 2023, pp. 145-160. https://link.springer.com/10.1007/978-3-031-32850-3_12
29. Andersen BL, Yang H, Farrar WB, et al: Psychologic intervention improves survival for breast cancer patients: A randomized clinical trial. Cancer 113:3450-3458, 2008
30. Lancellotta V, De Sanctis V, Cornacchione P, et al: HAPPY – Humanity Assurance Protocol in interventional radiotheraPY (brachytherapy) – an AIRO Interventional Radiotherapy Study Group project. J Contemp Brachytherapy 11:510-515, 2019
31. Basch E, Schrag D, Henson S, et al: Effect of electronic symptom monitoring on patient-reported outcomes among patients with metastatic cancer: a randomized clinical trial. JAMA 327:2413, 2022