

The Radiotherapy of Locally Advanced Esophageal Cancer of Inoperable Forms with Escalated Dose of 66-70 Gy

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Rezumat

Radioterapia cancerului esofagian local avansat al formelor inoperabile cu doză crescută de 66-70 Gy

Incidența cancerului esofagian în special cel de jonctiune esogastrică este în creștere datorită obezității și a refluxului gastric și reprezintă 90% a tumorilor esofagiene. Ghidul actual NCCN recomandă o doză totală de 50,4 Gy în fracțiuni de 1,8 Gy, doză insuficientă pentru obținerea unui control tumoral local. Noi prezentăm din experiența noastră 3 cazuri în care am aplicat într-un tratament combinat cu chimioterapia o doză totală la nivelul tumorii primare 66-70 Gy în fracțiuni de 2 Gy. Descriem critic metodele de investigare cu accentuarea rolului examinării PET/CT în stabilirea volumului țintă pentru o radioterapie curativă. Toate cazurile au fost tratate cu o radiochimioterapie. Cazurile prezentate au primit o doză curativă de 66-70 Gy în fracționare standard la nivelul tumorii primare. Technica de iradiere a fost cea de IMRT tip VMAT. Cele 3 cazuri proprii de tumori esofagiene la nivelul esofagului extratoracic, intratoracic sau de jonctiune esogastrică care au tratate în combinație cu o chimioterapie și la care a fost aplicată la nivelul tumorii primare o doză totală de 66-70 Gy în fracționare standard. La cele 3 cazuri prezentate a fost obținut un control tumoral și pacienții au supraviețuit ani de zile. În ciuda recomandărilor din literatura de specialitate o tumoră esofagiană indiferent de localizarea ei în esofagul extratoracic, intratoracic sau la nivelul jonctiunii esogastrice, prin utilizarea tehnicii de radioterapie cu intensitate modulată și prin aplicarea unei doze totale de 66-70 Gy în 33-35 de fracțiuni este local vindecabilă.

Cuvinte cheie: cancer esofagian, radioterapie, volum țintă, doză curativă, 70 Gy, supraviețuire

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Abstract

Squamous cell carcinoma and adenocarcinoma account for more than 90% of all esophageal cancer cases. The total dose recommended in the actual NCCN guidelines is 50.4 Gy in 1,8 Gy fractions for the treatment of an esophageal cancer, a dose who never cure a macroscopic tumor. We present here 3 clinical cases where we delivered 66-70 Gy in 2 Gy fraction and a local cure was obtained. We examine and describe critically the role of curative radiotherapy for the management of esophageal cancer or combined with other modalities. Each patient had a PET/CT examination before starting the curative treatment. We also describe and present the role of radiation technologies and the concept of target volume delineation for the different parts of the esophagus as extrathoracic, intrathoracic and the eso-gastric junction. We present clinical cases of extrathoracic, intrathoracic and an esophageal junction cancer who were treated with curative intent by applying a combined radiochemotherapy with a total dose of 66-70 Gy in 33-35 fractions. Despite of the data from the literature the local cure of an esophageal cancer in the extrathoracic, intrathoracic or at the eso-gastric junction by using IMRT technics and by applying a total dose of 66-70 Gy in standard fractionation is possible.

Key words: esophageal cancer, radiotherapy, target volume, curative dose, 70 Gy, survival

Case Presentations from our Own Experience

The radiation treatment of locally advanced esophageal cancer is very controversial. The actual guidelines recommend not more than 50.4 Gy in standard fractionation of 1.8 Gy. The longterm results in locally advanced or inoperable esophageal cancer are very disappointing as very rare locally cured patients survive more than 3 years the primary treatment. In the late eighties we introduced the target volume delineation concept in the radiation oncology (1). Specially inoperable or locally advanced esophageal cancer patients were irradiated with a larger total dose than 50.4 Gy as recommended in the guidelines.

We present here three cases in which patients were successfully treated with a total dose applied to the primary esophageal cancer of 66-70 Gy in standard fractionation.

Extrathoracic Esophageal Cancer

Our first case presented here is a 52-year-old patient, who was diagnosed with esophageal cancer in the extrathoracic esophagus near the mouth of the esophagus. Histopathological examination (3.2010) described a squamous

carcinoma, grading G3. The recommendation of the tumor board was to apply a combined treatment (radiochemotherapy) with a total dose of 70.2 Gy - after a 2-cycle induction chemotherapy with Cyclophosphamide and 5-Fu. Cisplatin radiochemotherapy (100 mg) followed in weeks 1-5 and irradiation with IMRT (VMAT) technique with 1.8 Gy to a dose of 52.2 Gy in 1.8 Gy fractions. The boost was applied with 18 Gy in 10 fractions of 1.8 Gy by Step & Shout technique. The irradiation plan of the application of the 52.2 Gy and of the overprint by 18.2 Gy is shown in *Fig. 1*.

9 years after the primary treatment, the patient is in complete remission and continues to practice his profession.

Intrathoracic Esophageal Cancer

Our next case was of a relatively young patient (63 years old) who underwent radiochemotherapy for a lower esophageal tumor located (in the lower third of the esophagus) at 35 cm from the dental arch. The clinical stage was cT2 cN0 M0. The patient was from the surgical point of view inoperable. Histopathological examination confirmed the presence of squamous carcinoma G2. Simultaneously he

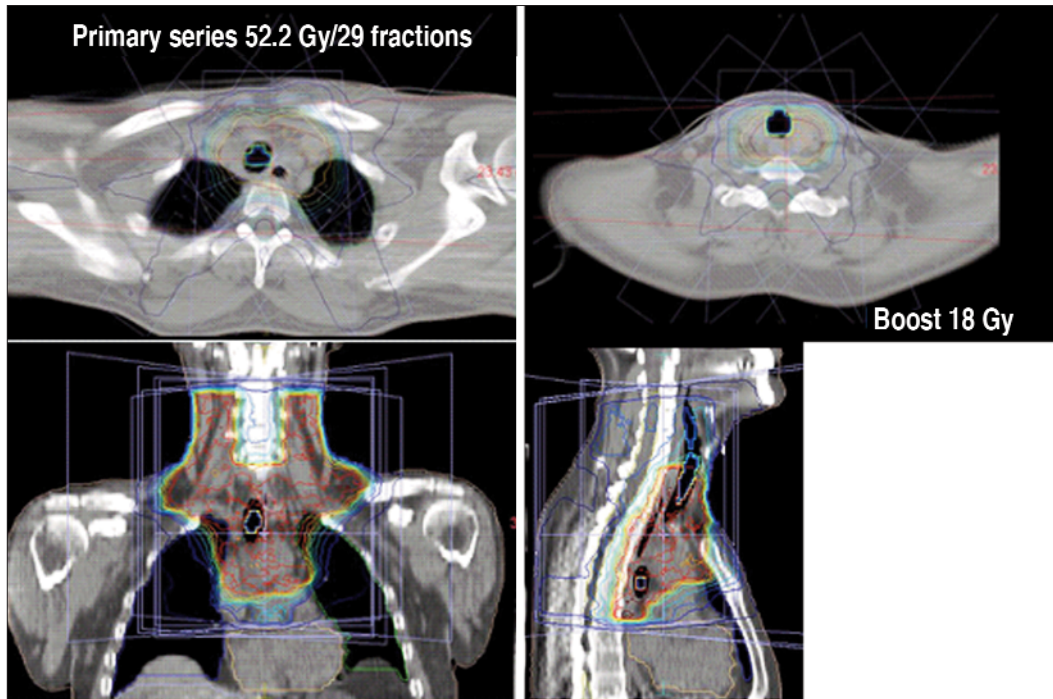


Figure 1. VMAT irradiation plan for extrathoracic localized esophageal cancer. The total dose applied to the primary tumor was 70.2 Gy in 1.80 Gy fractions. Microscopic disease of the cervical lymph nodes and upper mediastinum was irradiated with a total dose of 52.2 Gy / 1.8 Gy

followed a supportive care treatment with a hypercaloric nutrition for the constant maintenance of weight throughout the therapy. The target volumes used and the applied irradiation technique made it possible to apply a total dose of 70 Gy in 35 fractions on the primary tumor (red line) and 50 Gy on the tributary (mediastinal) lymphatic areas (green line). The applied radiotherapy plan using technical IMRT (VMAT) is presented in *Fig. 2*.

The image above shows the distribution of applied irradiation isodoses. In the axial section the magenta surface includes the mediastinum with microscopic disease. On this volume a dose of 50 Gy is applied in 25 daily fractions. In the sagittal and coronary sections, the thick red line marks the area that includes the primary tumor. On this volume were applied 70 Gy in 35 fractions. After curing the esophageal cancer, the patient lived another 3 years in which he was treated for other two primaries: a head and neck cancer and a lung cancer.

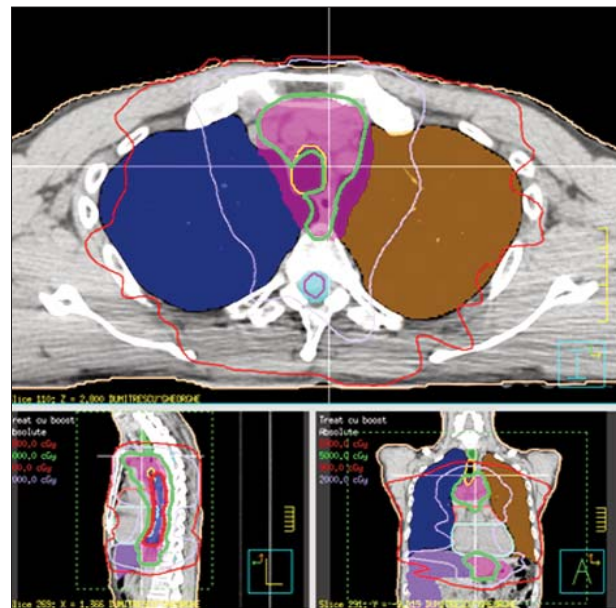


Figure 2. The irradiation plan of a patient with an esophageal tumor at the level of subcarinal portion. The irradiation plan, axial, sagittal and coronary section by the target volume, on which a total dose of 50 Gy was applied in fractions of 2.0 Gy. At the primary cancer 70 Gy were delivered.

Distal Esophageal Cancer: Eso-Gastric Junction Cancer

Our third case presented here is of a 71-year-old old patient. He was diagnosed with an inoperable stage III (cT2 cN2 M0) eso-gastric junction adenocarcinoma (at 35 cm from the incisors). The systemic neoadjuvant treatment was (Docetaxel (d1), Oxaliplatin (d1) and Capecitabine (d1–6) q2w followed by VMAT radiotherapy. The clinical target volume (CTV) for irradiation of an esophageal junction cancer included the microscopic disease of the mediastinal lymph nodes and upper abdomen, as well as the junction tumor. The gross tumor volume (GTV) included the macroscopic tumor highlighted by imaging methods (CT, PET/CT) as well as the information from the barium swallow examination of the transit through the junction area. The treatment was a combined radio-chemotherapeutic one and was started only if the patient's nutrition care could be also provided parenterally during the whole treatment through a PORT system. Weighing the patient and monitoring the nutritional status was mandatory.

In the *Fig. 3* is represented the irradiation plan with VMAT technique used at the AMETHYST Radiotherapy Center, Otopeni.

Two years after the end of radio-chemotherapy, the patient is in complete remission. During the 7-weeks radio-chemotherapy the patient was fed by the care of the nutrition team and had a weight loss of only 2 kilograms.

Conclusions

The progress made on multiple levels, namely medical through new techniques of surgery, imaging (CT, PET/CT), radiotherapy equipment with dose application procedures under daily imaging control and more effective chemotherapy schemes, have achieved that impact that offers patients with an esophageal cancer a higher chance of survival. Nutrition during radiochemotherapy is mandatory and

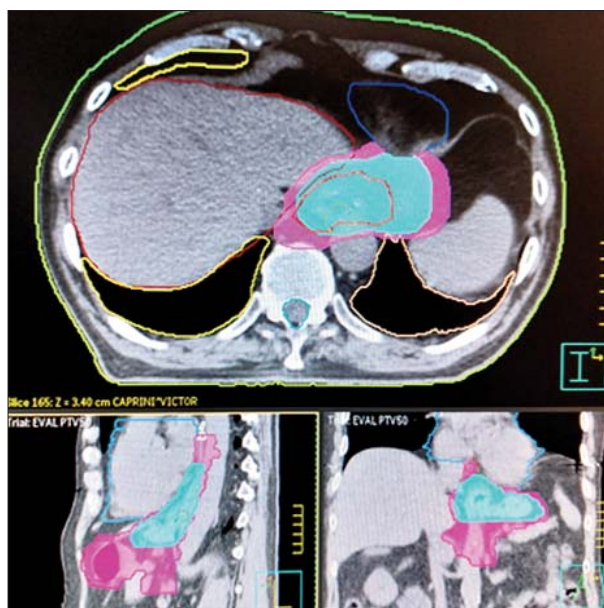


Figure 3. Irradiation plan with VMAT technique: axial, sagittal and coronary section through the patient's chest at the subcarinal/supra-diaphragmal level of the subcarinal region where the green line represents isodosis of 50 Gy and the red line on that of 66 Gy. The green surface is the macroscopic tumor and the red surface is the area with microscopic disease

makes it possible to apply the treatment without interruptions. A total dose of 66-70 Gy on the primary esophageal cancer offer the chance of local cure.

The treatment in the multidisciplinary team, based on the decision taken by the tumor board of patients with esophageal cancer, is a reflection of the degree of civilization of society and ultimately those responsible for the life of patients, namely the medical staff and doctors in the first place.

Conflicts of Interests

The author declare that they have no conflict of interest.

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