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# SIGMOID COLON ADENOCARCINOMA IN A PATIENT WITH SYNCHRONOUS PROSTATE ADENOCARCINOMA WITH COMPLETE THERAPEUTIC RESPONSE: CASE REPORT AND LITERATURE REVIEW

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***Keywords:*** *prostate, sigmoid, adenocarcinoma*

***Abstract:*** *Introduction: Over the last years, the incidence of multiple primary neoplasms has been increasing, with cases of primary prostate cancer and primary colorectal cancer being one of the most frequent. Case report: In the case of a 67-year-old patient with sigmoid cancer, a prostate cancer was found in pre-therapeutic imaging evaluations, later confirmed by histopathological examination. After colectomy with lymphadenectomy, he had received adjuvant chemotherapy, which was stopped because of persistent thrombocytopenia. A prostatectomy with lymphadenectomy was performed. After six months, Pet-PSMA showed bone lesions, so CyberKnife radiotherapy was performed on each. After another six month-free interval, the patient presented biochemical recurrence, so adjuvant "salvage" radiotherapy was performed with PSA value decreasing afterwards. Without hormonal therapy, which was declined for the moment by the patient, after six months, Pet-CT evidenced metastatic bone lesions and a secondary liver determination. Complete androgenic blockade type hormone treatment has been initiated, as well as chemotherapy, with imagistic complete response and stationary PSA value. Conclusions: In the cases of patients suffering from multiple cancers, serial and multimodal treatments are the only one able to ensure their healing, respectively their long-term survival.*

## INTRODUCTION

Colorectal cancer is the second leading cause of death in the United States and the fourth most frequently diagnosed cancer worldwide.(1,2) Despite that, the incidence decreased from 60.5 (in 1976) to 38.7 (in 2016) per 100.000 people. The mortality rates are also decreasing because of prevention, screening and treatment modalities. Half of diagnosed patients develop further metastases, especially liver metastases.(3) After local treatment, 50%-60% of the patients develop liver metastases, 20%-34% being declared with liver metastases at diagnosis.(4) Based on the Sheer Database, survival rates after 5 years are 91% to localized disease, 72% regional disease and 17% in a metastatic setting, so a combined 63% of patients were alive after 5 years.(5) In more than 50% of patients with colorectal cancer, autopsy often reveals liver metastases, which is the primary cause of death.(6) Prostate cancer is the fifth leading cause of cancer death among men worldwide and the second most frequently cancer diagnosed in men.(7,8) The incidence had been declining in the past years, based on screening attributed to prostate-specific antigen (PSA).(9) Prostate cancer frequently metastasis to bones and lymph nodes or directly infiltrates the bladder or the ureters.(10) It can metastasize to liver and brain.(11) For the patient diagnosed with local or loco-regional prostate cancer, 5 years survival rate arrives at 98% of the cases, although in metastatic disease 5-year-survival is only 30% of the cases.

## AIM

The aim of this study is to present the importance of multimodal treatment in a patient who had two different cancers at the same time: a sigmoid adenocarcinoma and a prostate cancer.

## CASE REPORT

We present the case of a 67-year-old male patient who presented to Gastroenterology Department in 2019, with a 3-month history of bloating, abdominal discomfort and unintentional weigh loss (10 kilograms in 5 months), accusing rectal bleeding, occasional with mucus and urinary incontinence. The patient's medical and social history was not significant. Colonoscopy performed in 2019 revealed a proliferative, friable, stenotic tumour, with a suspect appearance of malignancy. Tumour was localized at 60 cm from the anal orifice. Biopsies taken, confirmed the diagnosis of well-differentiated infiltrative adenocarcinoma. CT thoracic, abdomen and pelvic scans showed a stenotic tumour of 48/34 mm, at the sigmoidian level, with fat infiltration, prostate showed a transverse diameter of 53 mm, inhomogeneous structure, with calcifications, minimal ascites, perisigmoidian lymphadenopathy up to 8 mm, a process of osteosclerosis with inhomogeneous character at the level of the spongy L3 vertebra, possibly hemangioma. Initial PSA was 4 times the normal value, 16 ng/dl (normal value <4ng/dl), unknown value for Carcinoembryonic antigen (CEA) and

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Carbohydrate antigen 19-9 (CA199) markers.

Pelvic MRI revealed a dimensionally enlarged prostate of 56/45 mm, with a tumour mass invading half right of the prostate almost entirely, with interest of the base, middle area and apex, with 30/40 mm diameter, proximal sigmoid stenotic tumoral process, 7 cm long, with overcoming of the serosa and infiltration of the adjacent adipose tissue, without lymphadenopathy, bone contrast at the level of the left iliac wing of 23 mm, nonspecific, without diffusion restrictions.

Prostate biopsy puncture revealed bilateral prostate adenocarcinoma, Gleason score 4 + 3 = 7, grade 4, 70%, grade 3 group (apex, median, right lobe base, left lobe median).

Sigmoidian segmental resection was performed with terminal colon-colic anastomosis, performed manually in double layer. Intraoperatively, there was observed a hard palpation tumour formation, of 5/5 cm, at the level of the sigmoid loop, with serous invasion, without other macroscopic changes. The definitive histopathological (HP) exam showed a G2 adenocarcinoma, which infiltrates all layers of the colonic wall to the serosa, without overcoming it, intratumoral necrosis present in 5% of the tissue sample, areas of abscess around a fistulisation area, intralymphatic invasion present, no venous or perineural invasion, free resection margins, 35 lymph nodes excised of which 2 with adenocarcinoma metastases, (pT3N1bMxL1Vo stage tumour).

Post-operative CA199 value was normal, ACE slightly increased (3,52ng/ml, normal value <3ng/ml). Whole body MRI presented hypertrophic prostate, large size, with malignant tumour signal abnormalities, affecting the central and peripheral area of the right lobe, the capsule appeared irregular and discontinuous, possible extracapsular extension, irregular area of the left iliac wing nonspecific, right frontal extranevraxial tumour with vasogenic edema and mass effect on the cerebral parenchyma, possibly meningioma.

Due to the cerebral MRI result, a right supraorbital minicraniotomy was performed with the tumour ablation, guided by neuronavigation, total ablation of Simpson II, dura mater plasty. The histopathological examination of the specimen showed a meningothelial meningioma grade I WHO. The immunohistochemistry assay showed CD34, CK AE1 / AE3, GFAP, S100, CD34 negative, EMA positive, KI67 <1%.

Radical prostatectomy with excision of seminal vesicles was performed at 3 months after the neurosurgical intervention with lymphadenectomy (12 lymph nodes). The anatomo-histopathological result showed prostate adenocarcinoma, Gleason score 7 (4 + 3), group 3(based on WHO 2016 Staging), perineural intraprostatic invasion, which infiltrates the fat tissue at the right base and the right seminal vesicle, with venous invasion, pT3a+bN1bMxL0V1R0. Post operatory PSA was within the normal range (0.11ng/ml).

Post operatory thoracic, abdomen and pelvis computer tomography does not highlight any pathological changes.

**Figure no. 1. Postoperative pelvic MRI without any pathological changes, other than post-operative scar**

Based on the fact that there were negative factors at the pathological report from hemicolectomy such as: intratumoral necrosis, abscess, invasion of the lymph vessels, 2 lymph nodes with adenocarcinoma metastases, it was decided to administrate adjuvant chemotherapy for 6 cycles, CapeOx protocol: Capecitabine 1000mg/m2, twice a day, days 1-14, oral administration, tablets of 500 mg and Oxaliplatin 130mg/m2, intravenous infusion in 500 ml glucose 5%, over 120 minutes, repeated after 21 days. 3 cycles of CapeOx adjuvant chemotherapy were administered, subsequently delayed due to persistent thrombocytopenia, grade I and II.

After three months, PSA was 0.41ng/ml (normal value <4ng/dl), so it was interpreted as biochemical recurrence. Pet-PSMA showed 1 cm left iliac bone uptake and L2 transverse process, an uncertain D6 level. CyberKnife radiotherapy with 24 Gy/1 fr. was performed on each of the bone lesions, six months after radical prostatectomy. As a result, the PSA blood level was 0.187ng/dl (normal value <4ng/dl).

Loco-regional rescue radiotherapy was performed with Elekta Infinity Device, type 2020, VMAT-SIB technique, (volumetric modulated arc therapy - simultaneous integrated boost), total dose of 66 Gy/ 33 fr., 2 Gy/fractions on the prostate lodge, 52 Gy/26 fr., 1.8 Gy/fraction on the pelvic lymph nodes, tolerated with radio-dermatitis grade I, three month after CyberKnife radiotherapy .

Patient initially refused hormonal treatment, although PSA value had begun to increase, to 0,214ng/dl, 4,53ng/dl and 8,094ng/dl, (normal value <4ng/dl).

After 6 months, the abdominal pelvic MRI and Pet-CT with fluorodeoxyglucose showed secondary bone determination to L5, L3 right scapular spine, right iliac, CD D12, L1 and liver metastases of maximum 16 mm. versus diffraction of the liver, mediastinal lymphadenopathy of 15 mm.

**Figure no. 2. Liver metastases on abdominal pelvic MRI**

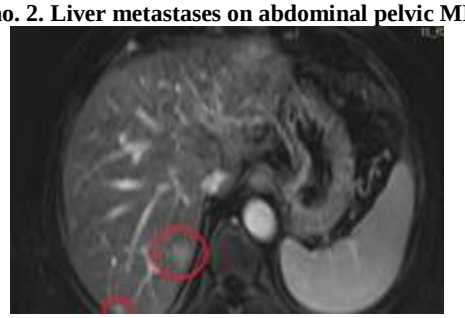
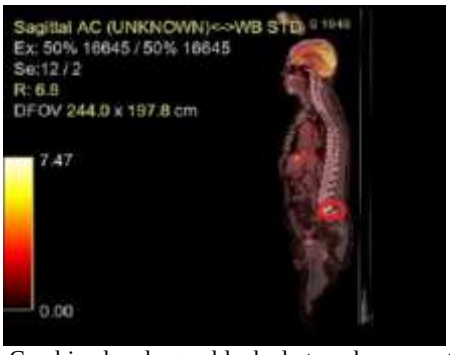


**Figure no. 3. Secondary bone determination of L5, on PET-CT**




Combined androgen blockade type hormone treatment had been initiated, when PSA value became 8.094ng/dl, with antiandrogen Bicalutamide 50 mg/day, tablets, oral administration for 14 days, then LH-RH agonist Leuprorelin 22.5 mg, injection, subcutaneous administration, one injection for three months.

**Figure no. 4. Secondary liver determination on PET-CT**

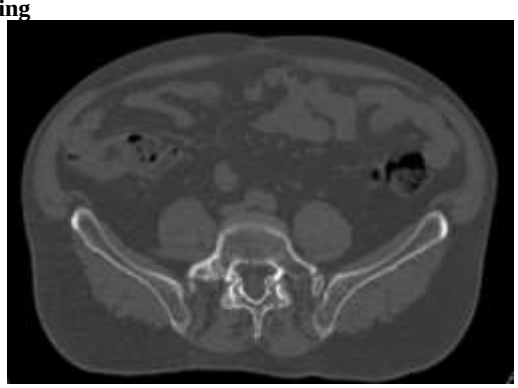

Given the disease-free interval of more than 1 year, as well as the metastatic stage, chemotherapy and targeted therapy were administered Folfox + Panitumumab (K -Ras and N-RAS wild type, Braf Wild type), 6 cycles, protocol: Panitumumab 6 mg/kg intravenous infusion in 100 ml sodium chloride 0.9% over 60 minutes, Oxaliplatin 85mg/m2 intravenous infusion in 500 ml glucose 5% over 120 minutes, Folinic Acid 400 mg/m2 intravenous infusion in 250 ml glucose 5% over 120 minutes, 5 Fluorouracil 400 mg/m2 intravenous bolus over 10 minutes and 5 Fluorouracil 2400 mg/m2 intravenous infusion, over 46 hours, by port-a-cath system. In the last 2 cycles, the patient presented a thrombocytopenia that required postponing treatment by up to one week. It was given sea buckthorn daily.

Imaging evaluation at the end of chemotherapy consisted of CT scan of the chest, MRI of the abdomen and pelvis which did not reveal any metastases, the PSA value was 0,038ng/dl, (normal value <4ng/dl). Hormone therapy with LH-RH analogue was continued. Due to persistent grade II thrombocytopenia, maintenance treatment could not be administered.

Hematological examination and specific blood tests for chronic infections found no other cause for thrombocytopenia, than chemotherapy. The hematologist prescribed corticoids, which improved thrombocytopenia to grade I: 80000-90000/ml, (normal value 150000-450000/ul).

After 6 months, PSA level was 1,564ng/dl, the abdominal-pelvic MRI revealed post-radiotherapy changes at the lumbosacral level, but with small hyper Stir images in the sacrum area, right paramedian, acetabular and pubic areas, possibly small secondary determinations or osteoporosis. That is why a bone scintigraphy was performed, which revealed secondary bone metastases in the right scapular spine, left vertebral hemi body of L3 vertebra, right L5 transverse process. Pet-PSMA confirmed the lesions highlighted on scintigraphy, which is why CyberKnife radiotherapy with 24 Gy/1 fr. was performed, on each of the bone lesions.

**Figure no. 5. Secondary bone determination on CyberKnife imaging**



Both CT thoracic scans and abdominal-pelvic MRI showed a complete therapeutic response without distant metastases, tumour markers being within the normal limits (ACE, CA199 and PSA=0.281ng/dl). PET CT performed at 6 months afterward did not give evidence of a malignant disease.
So far, the imaging reassessment has been performed at 3 and 6 months, maintaining the complete imaging response and the values of the markers, PSA till now up to 0.32ng/dl. Also, the RH-LH analogue hormonotherapy is continued.

## DISCUSSIONS

Two primary neoplasms in different organs represents the existence of two cell type tumours and are known as Multiple Primary Tumours (MPT).(12) This occurs between 5% and 8% of all cancers, the most frequent association being prostate-colorectal (26%). But, there are cases cited in literature of colorectal cancers associated with gastric cancer, breast cancer, or lung cancer.(13)

Because every cancer type has different symptoms and a different therapeutic circuit, every case needs a multimodal treatment and personalized approach. There are quite a few cases cited in the literature of patients with sigmoid cancer who also have cancers located outside the digestive tract. It was observed that 2%-5% of colorectal cancers were detected in patients with Lynch syndrome. This syndrome is characterized by the association of familial colorectal cancers associated with extra-colonic neoplasms.(14,15) Lynch syndrome occurs due to the existence of mutations in the MMR genes, which causes in the case of tumour cells the appearance of microsatellite instability as well as a decrease in the cellular expression of proteins that are encoded by the MMR gene.(16) Mutations in this gene can be detected by immunohistochemical studies. In recent years, in the oncologic centres from the United States, all patients with colorectal cancer have been screened for the existence of the Lynch syndrome.(17) In our case, the existence of Lynch syndrome was ruled out.

In our case, patient had synchronous cancer at colon and prostate. Colon cancer gave hepatic metastases and prostate cancer gave bone metastases. The main treatment, for hepatic metastases in colon carcinoma is the complete hepatic metastases resection, with an adequate hepatic function remaining.(18-19) There are no recommendations for debulking resection. In the other cases, ablative techniques may be considered, such as periportal vein embolization, radioembolization or staged liver resection.(20-22)

Hepatic arterial infusion is a procedure where chemotherapy injection is practiced directly into the branches of the hepatic artery, using a port or implantable device, on the hepatic artery. This approach can lead to malignant cell destruction.(23) Chemoembolization consists in catheterizing the hepatic artery where chemotherapy will be administered, later reaching the occlusion of the hepatic artery which irrigates the hepatic tumour.(24) Based on the fact that high radiation leads to ionic agitation, heat and can produce coagulative necrosis, radio embolization is another local therapy used in these cases. Based on a meta-analysis of 90 studies, all three techniques lead to same results.(25)

In our patient, because of the mediastinal lymphadenopathy, we had considered the disease to be unresectable in that moment, so we initiated aggressive chemotherapy for conversion to resectability. In the future, if the patient will develop only hepatic metastases, we can use ablative techniques. In case of extrahepatic disease, dependent on free disease interval, we will use the same chemotherapy and targeted therapy, or FOLFIRI+Bevacizumab protocol, depending of thrombocytopenia.

Despite the fact that many high-risk patients with

prostate cancer develop bone metastases, it is recommended to use Bisphosphonates only after the disease is hormone-resistant, or the patient is symptomatic.(26) Local radiotherapy in prostate cancer is used in local or loco-regional advanced disease. In high and intermediate risk patients with an aggressive tumour type, we can use prophylactic lymph node irradiation. In our case, due to the fact that there was lymph node invasion on pathological report, and there was an extension of the tumour beyond the prostate, the patient was in high risk category so it was necessary to perform lymph node irradiation, despite higher toxicity.(27)

Volumetric modulated arc therapy (VMAT) is an improvement from intensity modulated radiotherapy (IMRT) and has the great advantage of an equal dose distribution with less toxicity.(28) Considering that our patient had over 4 bone metastases the second time, with one beyond the pelvis, we can say that it was a disease with an increased tumour volume. Stereotactic body radiation therapy (SBRT) is a therapeutic method which administers high doses of treatment with lower toxicity and great precision frequently with CyberKnife.(29) This method identifies the location of the prostate during treatment and makes active corrections in terms of movements of the prostate during treatment delivery.(30) This radiotherapy technique is not available in our country that is why, it was performed abroad.

After a discussion with the patient and his family, given the one-year free interval between the appearance of bone lesions, and the oligometastatic disease, after a discussion in tumour board, we recommended Cyberknife ablative radiotherapy.

First literature data which described oligometastatic disease were in 1995.(31) It represents the moment when the cancer cells leave the primary tumour forming other small metastases, without being a clear definition of the maximum number of metastases. In prostate cancer, oligometastatic disease is considered in generally as maximum of 3 metastases in bone or lymph nodes only, but other criteria have used up to six.(32) Every patient with oligometastatic disease can be treated with SBRT, regardless of location, given the big advantage of minimal toxicity and minimal side effects.(33) The procedure is well tolerated even by elderly patients.(34) Local control and pain reduction is up to 90%.(35) The disadvantages of this technique are the selection of patients, as well as the lack of treatment centres, altogether being an expensive and complex technique.(36)

CyberKnife radiosurgery provided a feasible approach to control the oligometastatic disease of this patient. Local control of distant metastasis was achieved while still sparing normal tissues as much as possible, while also giving the option of a later re-irradiation in the vicinity should new lesions arise. CyberKnife treatments are usually performed in 1 to 5 sessions, with a total dose between 6-45 Gray ranges, of 6-15 Gray each.(37) Both in the literature and in our case, initially an attempt was made to delay systemic treatment, given the cardiovascular risks associated with ADT therapy.(38)

Once colon cancer patients have fully responded, they need maintenance treatment to prevent the disease from progressing. Meta-analyses have shown that in cases where a single liver metastasis was resected, overall survival at 5 years was 71%.(39) This approach was not feasible in our case, because of mediastinal lymph nodes disease. There are limited data in the literature which analyse the resection or local treatments of extrahepatic metastases, in the metastatic colon cancer. The most important factor which can predict the survival, is the primary localization of the tumour. Left side tumours have better prognostic than right side tumours, overall survival vary from 40% to 20% at 5 years.(40,41) In prostate cancer, once the patient develops metastases, overall survival is on average 4 years, based on anatomopathological findings, tumour volume and PSA doubling time. In metastatic settings, based on PSA value after seven months of androgen deprivation therapy, if PSA is maximum 0,2 ng/dl, the patient is in low risk category, median survival of 75 months, intermediate risk category with a PSA between 0,2-4ng/dl, median survival of 44 months, and at high risk with a PSA above 4 ng/ml, with median survival of 13 months.(42)

If the complete response will maintain, our goal is to give maintenance treatment for colon cancer. In prostatic cancer, the disease will eventually evolve to PSA rise and eventually bone metastases, when we can add Bisphosphonates, while in case of symptoms, hormonal treatments like Abiraterona, Enzlutamida, or chemotherapy Docetaxel.

Nowadays, treatment of patients with multiple cancers of the digestive tract and extra digestive organs is not standardized in terms of surgery. There are oncology centres that perform this kind of surgeries at the same time as initial surgery, but there are also centres that perform serial surgeries. The same thing happened in our case. Supporters of the idea of practice of a multidisciplinary team surgery are based on the fact that reducing the number of the surgical interventions can lead to a decrease in morbidity, respectively postoperative mortality, as well as reducing the period between surgery and the initiation of adjuvant cancer therapy.(43)

The particularity of the case consists in the fact that two types of cancers were diagnosed in the same patient with a complete imaging response to treatment, which is maintained despite the fact that until now, it has not been possible to resume chemotherapy and targeted maintenance therapy, due to secondary thrombocytopenia.

## CONCLUSIONS

In the cases of the patients suffering from multiple cancers, serial and multimodal treatments are the only one that are able to ensure their healing, respectively their long-term survival.

## REFERENCES


1. Siegel RL, Miller KD, Jemal A, Cancer statistics, 2020, CA Cancer J Clin. 2020 Jan;70(1):7-30. doi: 10.3322/caac.21590.
2. Cheng L, Eng C, Nieman LZ, Kapadia AS, Du XL, Trends in colorectal cancer incidence by anatomic site and disease stage in the United States from 1976 to 2005, Am J Clin Oncol. 2011 Dec;34(6):573-80. doi: 10.1097/COC.0b013e3181fe41ed.
3. Lee WS, Yun SH, Chun HK, Lee WY, Yun HR, Kim J, et al. Pulmonary resection for metastases from colorectal cancer: prognostic factors and survival, Int J Colorectal Dis. 2007 Jun;22(6):699-704. doi: 10.1007/s00384-006-0218-2. Epub 2006 Nov 16.
4. Muratore A, Zorzi D, Bouzari H, Amisano M, Massucco P, Sperti E, et al. Asymptomatic colorectal cancer with un-resectable liver metastases: immediate colorectal resection or up-front systemic chemotherapy? Ann Surg Oncol. 2007 Feb;14(2):766-70. doi: 10.1245/s10434-006-9146-1. Epub 2006 Nov 14.
5. American Cancer Society. Cancer Facts & Figures 2021. Atlanta, Ga: American Cancer Society; 2021.
6. Foster JH, Treatment of metastatic disease of the liver: a skeptic's view, Semin Liver Dis. 1984 May;4(2):170-9. doi: 10.1055/s-2008-1040656.
7. Forman D, Ferlay J. The global and regional burden of cancer Organization WH: World Cancer Report 2014. Chapter 1.1. ISBN 9283204298.

8. Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012, Int J Cancer. 2015;136(5):E359-E386.
9. Herget KA, Patel DP, Hanson HA, Sweeney C, Lowrance WT, Recent decline in prostate cancer incidence in the United States, by age, stage, and Gleason score, Cancer Med. 2016 Jan;5(1):136-41. doi: 10.1002/cam4.549. Epub 2015 Dec 2.
10. Reigman HI, Stokkel MP. Peripheral bone metastases in prostate cancer: a rare localization at initial presentation. Clin Nucl Med. 2004;29(5):335–336. doi: 10.1097/01.rlu.0000123327.62553.d0.
11. Zhao F, Wang J, Chen M, et al. Sites of synchronous distant metastases and prognosis in prostate cancer patients with bone metastases at initial diagnosis: a population-based study of 16,643 patients. Clin Transl Med. 2019;8:0.
12. las Heras Alonso MM, Más AG, Independent multiple primary tumors and second primary neoplasms. Relationship between smoking Actas Urol Esp. 2010;34(6).
13. Kan JY, Hsieh JS, Pan YS, Wang WM, Chen FM, Jan CM, et al. Clinical characteristics of patients with sporadic colorectal cancer and primary cancers of other organs., Kaohsiung J Med Sci. 2006 Nov;22(11):547-53. doi: 10.1016/S1607-551X(09)70351-1.
14. Liu W, Zhang D, Tan SA, Liu X, Lai J. Sigmoid Colon Adenocarcinoma with Isolated Loss of PMS2 Presenting in a Patient with Synchronous Prostate Cancer with Intact MMR: Diagnosis and Analysis of the Family Pedigree., Anticancer Res. 2018 Aug;38(8):4847-4852. doi: 10.21873/anticanres.12796.
15. Boland CR, Koi M, Chang DK, Carethers JM. The biochemical basis of microsatellite instability and abnormal immunohistochemistry and clinical behavior in Lynch syndrome: from bench to bedside. Fam Cancer. 2008;7:41-52.
16. Parsons R, Li GM, Longley MJ, Fang WH, Papadopoulos N, Jen J, et al. Hypermutability and mismatch repair deficiency in RER+ tumor cells. Cell 75; 1993. p. 1227-1236.
17. National Comprehensive Cancer Network. Genetic/familial high-risk assessment: colorectal (version 2.2016). Available at: www.nccn.org/professionals/physician_gls/pdf/genetics_colon.pdf. Accessed on November 11, 2016.
18. Abdalla EK, Vauthey JN, Ellis LM, et al. Recurrence and outcomes following hepatic resection, radiofrequency ablation, and combined resection/ablation for colorectal liver metastases Ann Surg. 2004 Jun;239(6):818-25; discussion 825-7. doi: 10.1097/01.sla.0000128305.90650.71.
19. Charnsangavej C, Clary B, Fong Y, Grothey A, Pawlik TM, Choti MA. Selection of patients for resection of hepatic colorectal metastases: expert consensus statement, Ann Surg Oncol. 2006 Oct;13(10):1261-8. doi: 10.1245/s10434-006-9023-y. Epub 2006 Sep 1.
20. Covey AM, Brown KT, Jarnagin WR, et al. Combined portal vein embolization and neoadjuvant chemotherapy as a treatment strategy for resectable hepatic colorectal metastases, Ann Surg. 2008 Mar;247(3):451-5. doi:10.1097/SLA.0b013e31815ed693.
21. Adam R, Miller R, Pitombo M, et al. Two-stage hepatectomy approach for initially unresectable colorectal hepatic metastases, Surg Oncol Clin N Am. 2007 Jul;16(3):525-36, viii. doi: 10.1016/j.soc.2007.04.016.
22. Teo JY, Allen Jr JC, Ng DC, et al, A systematic review of contralateral liver lobe hypertrophy after unilobar selective internal radiation therapy with Y90, HPB (Oxford). 2016 Jan;18(1):7-12. doi: 10.1016/j.hpb.2015.07.002. Epub 2015 Dec 11.
23. Kemeny N, Management of liver metastases from colorectal cancer, Oncology (Williston Park). 2006 Sep;20(10):1161-76, 1179; discussion 1179-80, 1185-6.
24. Johnston FM, Mavros MN, Herman JM, Pawlik TM, Local therapies for hepatic metastases, J Natl Compr Canc Netw. 2013 Feb 1;11(2):153-60. doi: 10.6004/jnccn.2013.0023.
25. Zacharias AJ, Jayakrishnan TT, Rajeev R, et al. Comparative Effectiveness of Hepatic Artery Based Therapies for Unresectable Colorectal Liver Metastases: A Meta-Analysis, PLoS One. 2015 Oct 8;10(10):e0139940. doi: 10.1371/journal.pone.0139940.
26. Tosoian JT, Chappidi M, Feng Z, et al. Prediction of Pathologic Stage Based on Clinical Stage, Serum PSA, and Biopsy Gleason Score: Partin Tables in the Contemporary Era. BJU Int. 2017 May;119(5):676-683. doi: 10.1111/bju.13573. Epub 2016 Jul 29.
27. Parker CC, James ND, Brawley CD, et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial, Lancet. 2018 Dec 1;392(10162):2353-2366. doi: 10.1016/S0140-6736(18)32486-3. Epub 2018 Oct 21.
28. Kopp RW, Duff M, Catalfamo F. VMAT vs. 7-field-IMRT: assessing the dosimetric parameters of prostate cancer treatment with a 292-patient sample, ed Dosim. Winter 2011;36(4):365-72. doi: 10.1016/j.meddos.2010.09.004.
29. Serra M, Ametrano G, Borzillo V, et al. Dosimetric comparison among cyberknife, helical tomotherapy and VMAT for hypofractionated treatment in localized prostate cancer, Medicine (Baltimore). 2020 Dec 11;99(50):e23574, DOI: 10.1097/MD.0000000000023574.
30. Kilby w, Dooley JR, Kuduvalli G, Sayeh S, Maurer Jr. CR, The CyberKnife® robotic radiosurgery system in 2010, Technology in Cancer Research and Treatment. 2010;9(5):433-452.
31. Hellman S, Weichselbaum RR. Oligometastases. J Clin Oncol. 1995;13:8-10. https://doi.org/10.1200/JCO.1995.13.1.8.
32. Gillessen S, Omlin A, Attard G, et al. Management of patients with advanced prostate cancer: recommendations of the St Gallen advanced prostate cancer consensus conference (APCCC) 2015. Ann Oncol. 2016;26:1589–1604. https://doi.org/10.1093/annonc/mdw180.
33. Tree AC, Khoo VS, Eeles RA, Ahmed M, Dearnaley DP, Hawkins MA, et al. Nutting CM, Ostler PJ, van As NJ. Stereotactic body radiotherapy for oligometastases. Lancet Oncol. 2013;14:e28–e37. https://doi.org/10.1016/S1470-2045(12)70510-7.
34. Sridharan S, Steigler A, Spry NAet al. Oligometastatic bone disease in prostate cancer patients treated on the TROG 03.04 RADAR trial. Radiother Oncol. 2016;121:98–102. https://doi.org/10.1016/j.radonc.2016.07.021
35. Muacevic A, Kufeld M, Rist C. Safety and feasibility of image-guided robotic radiosurgery for patients with limited bone metastases of prostate cancer, Urologic Oncology: Seminars and Original Investigations xx. 2011.
36. Tree AC, Khoo VS, Eeles RA, Stereotactic body radiotherapy for oligometastases,The Lancet Oncology. 2013;14(1):E28-E37.
37. Napieralska A, Miszczyk L, Stapor-Fudzinska M, CyberKnife stereotactic radiosurgery and stereotactic ablative radiation therapy of patients with prostate cancer bone metastases, Neoplasma. 2016;63(2):304-12. doi: 10.4149/218_150807N435.

38. Efstathiou JA, Bae K, Shipley WU, Hanks GE, Pilepich MV, Sandler HM, et al. Cardiovascular mortality and duration of androgen deprivation for locally advanced prostate cancer: analysis of RTOG 92-02. Eur Urol. 2008;54(4):816–823.
39. Aloia TA, Vauthey JN, Loyer EM et al. Solitary colorectal liver metastasis: resection determines outcome, Arch Surg. 2006 May;141(5):460-6; discussion 466-7. doi: 10.1001/archsurg.141.5.460.
40. Grothey A, Sargent D, Goldberg RM. Survival of Patients With Advanced Colorectal Cancer Improves With the Availability of Fluorouracil-Leucovorin, Irinotecan, and Oxaliplatin in the Course of Treatment, Journal of Clinical Oncology. J Clin Oncol. 2004 Apr 1;22(7):1209-14. doi: 10.1200/JCO.2004.11.037.
41. Hadden WJ, de Reuver PR, Brown K, Resection of colorectal liver metastases and extra-hepatic disease: a systematic review and proportional metaanalysis of survival outcomes, HPB. 2016;18(3):209-220.
42. Hussain M, Tangen CM, Higano C. Absolute prostate-specific antigen value after androgen deprivation is a strong independent predictor of survival in new metastatic prostate cancer: data from Southwest Oncology Group Trial 9346 (INT-0162), J Clin Oncol. 2006 Aug 20;24(24):3984-90. doi: 10.1200/JCO.2006.06.4246.
43. Imagami T, Takayama S, Hattori T, Matsui R, Sakamoto M, Kani H, et al. Combined laparoscopic and robotic surgery for synchronous colorectal and genitourinary cancer: A case series, Int J Surg Case Rep. 2018;51:323-327. doi:10.1016/j.ijscr.2018.09.021.