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Original article

# Stereotactic radiation therapy of brain metastases from colorectal cancer: A single institution cohort

## *Radiothérapie stéréotaxique des métastases cérébrales de cancer colorectal : une cohorte monocentrique*

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ABSTRACT

*Purpose.* – The brain remains an uncommon site of colorectal cancer metastases. Due to the improvement of overall colorectal cancer patient survival, the incidence of brain metastases will likely rise. We report the efficacy and safety of hypofractionnated stereotactic radiation therapy and stereotactic radiosurgery, and its role in colorectal cancer brain metastasis management.
*Methods and material.* – Between June 2010 and December 2014, fifteen consecutive patients received hypofractionnated stereotactic radiation therapy or stereotactic radiosurgery as first local therapy or following surgical removal for colorectal cancer brain metastases. The primary endpoint was overall survival. Secondary endpoints were brain progression free survival, in field control rates and safety.
*Results.* – Median follow-up was 41 months (95% confidence interval [CI]: [8.9–73.1 months]), median overall survival was 8 months (95% CI [4.7–11.3 months]), and median brain progression-free survival was 5 months (95% CI [3.9–6.1 months]). Five in field recurrences were observed, which makes a control rate per metastases at 6 and 12 months of 77.8% (95% CI [74.34%–81.26%]), 51.9% (95% CI [44.21%–59.59%]) respectively. Over the 19 treatment sequences, five in field recurences were observed: 6, 12 and 18 months control rate per treatment sequence were 93.3% (95% CI [90.42%–96.18%]), 68.1% (95% CI [62.03%–74.17%]) and 45.4% (95% CI [36.14%–54.66%]) respectively. Immediate tolerance was good with no toxicity grade III or more. Long-term toxicity included two radionecrosis among which, one was symptomatic.
*Discussion.* – The results of this retrospective analysis suggest that hypofractionnated stereotactic radiation therapy and stereotactic radiosurgery are effective and safe treatment modalities for single and multiple small brain metastases from colorectal cancer. However, results need to be confirmed by multicenter, collected data.


*Mots clés :*
Cancer colorectal
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RÉSUMÉ

*Objectif de l'étude.* – Le cerveau est un site peu fréquent de métastases de cancer colorectal. Il est probable que l'incidence des métastases augmente avec la survie globale des patients atteints de cancer colorectal. Nous rapportons l'efficacité, la sécurité et le rôle dans la prise en charge des métastases cérébrales de cancer colorectal de la radiothérapie en conditions stéréotaxiques hypofractionnée ou non fractionnée.
*Matériel et méthodes.* – Quinze patients consécutifs ont été traités ainsi pour des métastases cérébrales de cancer colorectal, soit en première intention, soit après chirurgie, entre juin 2010 et décembre 2014. Le critère d'évaluation principal était la survie globale. Les critères de jugement secondaires étaient la survie sans récidive cérébrale, le taux de contrôle dans le volume irradié et la tolérance.

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*Résultats.* – Le suivi médian était de 41 mois (IC 95 % [intervalle de confiance à 95 %]: 8,9–73,1 mois), la durée médiane de survie était de 8 mois (IC 95 % : 4,7–11,3 mois), celle de survie médiane sans récidive intracérébrale de 5 mois (IC 95 % : 3,9–6,1 mois). Cinq récidives locales ont été observées, le taux de contrôle local par métastase traitée était à 6 et 12 mois respectivement de 77,8 % (IC 95 % [74,34 %–81,26 %]) et 51,9 % (IC 95 % [44,21 %–59,59 %]). Sur les 19 séquences de traitement, cinq rechutes locales dans le volume irradié ont été observées, soit un taux de contrôle local par traitement respectivement à 6, 12 et 18 mois de 93,3 % (IC 95 % : 90,42 %–96,18 %), 68,1 % (IC 95 % : 62,03 %–74,17 %) et 45,4 % (IC 95 % : 36,14 %–54,66 %). La tolérance immédiate a été bonne, sans toxicité de grade III ou plus rapportée. La toxicité tardive a consisté en deux radionécroses, dont une était symptomatique.
*Discussion.* – Les résultats de cette analyse rétrospective suggèrent que la radiothérapie en conditions stéréotaxiques hypofractionnée ou non fractionnée sont des modalités efficaces et bien tolérées de traitement des métastases cérébrales uniques ou multiples de petite taille de cancer colorectal.


## 1. Introduction

Colorectal cancer is the third most common cancer in developed countries and is responsible for 12% of all cancer related deaths [1]. Almost 20% of patients suffering from colorectal cancer have metastases at the time of diagnosis; 25% of patients with colorectal cancer will develop metastases but only 1% will develop brain metastases [2,3]. However, the incidence of brain metastases in patients with colorectal cancer will likely increase as new systemic therapeutics became available and efficacious. Moreover, novel systemic therapies that do not cross the blood-brain barrier will also contribute to a higher rate of brain metastasis [4]. Brain metastases from colorectal cancer are always the last occurrence and poor prognostic factor of the disease, with median survival ranges from 1.0 to 5.7 months [5].

According to the American Society for Radiation Oncology guidelines, stereotactic radiosurgery and hypofractionnated stereotactic radiation therapy can be considered for single brain metastasis larger than 3 to 4 cm if surgically removed, for single metastasis smaller than 3 to 4 cm and for multiple metastases all smaller than 3 to 4 cm if the patient has a good prognosis (expected survival of 3 months or more) [6]. French ANOCEF guidelines proposed comparable indications but without special differentiation for colorectal cancer brain metastases [7,8].

Prognostic factors for patients with colorectal cancer brain metastasis include performance status, control of extracranial disease and age. Many scores have been developed to take into account those parameters: Recursive Partitioning Analysis (RPA), RPA II, Graded Prognostic Assessment (GPA), disease specific GPA (DS-GPA) and basic score for brain metastases (BSBM) [9–13].

This cohort study aims to report the practical use of stereotactic radiosurgery and hypofractionnated stereotactic radiation therapy in brain metastasis from colorectal cancers at our institution.

## 2. Materials and methods

### 2.1. Study design

This is a single-institution cohort study involving 15 patients consecutively treated from June 2010 to December 2014 for brain metastasis from colorectal cancer. Clinical data were retrieved from a university hospital database.

### 2.2. Patients

To be eligible for stereotactic radiosurgery or hypofractionnated stereotactic radiation therapy, patients must have met the following criteria:

- histologic diagnosis of primary colorectal cancer;
- less than 5 brain metastases;
- less than 50 mm in greater dimension.

Brain MRI was systematically performed less than 2 weeks prior to treatment. According to our institution protocol, patients underwent weekly clinical examination during treatment to evaluate toxicities; they received brain MRI and clinical examination 2 months after treatment to evaluate clinical and imaging response and toxicities.

### 2.3. Treatment technique

Each patient was immobilized in supine position using thermoplastic mask (BrainLab®, Munich, Germany). A CT scan without contrast injection was performed with 1.25 mm thickness slices. Two millimeters slice thickness MRI was performed for delineation less than 7 days before or after CT-scan. MRIs and CT scan were matched in the BrainLab software (Iplan 2.5, BrainLab®, Munich, Germany). For patients with non-resected metastases, the gross target volume (GTV) was delineated on the MRI with gadolinium enhancement. For patients who were treated following surgical resection, the clinical target volume included any residual tumor and the entire surgical cavity. The planning target volume (PTV) was defined as GTV + 2 mm, for unresected metastases or CTV + 2 mm, for resected metastases. Organs at risk included the eyes, lens, optical nerves, optical chiasm, inner ears, cochlea, brainstem, brain, pituitary gland and hippocampus (Table 1). Patients were treated with image-guided arc therapy (VMAT). Stereotactic radiosurgery and hypofractionnated stereotactic radiation therapy were delivered using a Novalis Tx® (Varian Medical System, Palo Alto, California) using three to five arcs with 6MV photons and daily ExacTrac image guidance. Dose limits applied to organs at risk are summarized in Table 2. Chemotherapy continuation remained at physician's discretion. Every patient have been following a corticosteroid therapy during treatment by prednisolone 60 mg per day, with a decrease of the dose during 6 days after the end of the radiotherapy.

### 2.4. Statistical methods

The number of patients included in this study was determined as any patient treated during the interval of the study and meeting the selection criteria. Data collection was performed by one person using a university hospital database. The primary endpoint of the study was overall survival, defined as the time between the beginning of the radiation therapy treatment and the date of death from any cause. Secondary endpoints included brain progression-free survival (BPFS), defined as the time between the beginning of