



# The experience of pain and anxiety in rectal cancer patients during high-dose-rate brachytherapy

*S. Néron PhD,\* S. Perez BSc,<sup>†</sup> R. Benc RN,<sup>‡</sup> A. Bellman,<sup>‡</sup> Z. Rosberger PhD,\* and T. Vuong MD<sup>§</sup>*

## ABSTRACT

### Background

Pain and anxiety have been reported as primary concerns for patients with head-and-neck, gynecologic, and prostate cancers undergoing high dose rate (HDR) brachytherapy. However, almost no research has been published on the degree to which these symptoms are experienced by rectal cancer patients undergoing HDR brachytherapy. We conducted a pilot study examining the experiences of rectal cancer patients during HDR brachytherapy, specifically the intensity and trajectory of their anxiety and pain.

### Methods

Rectal cancer patients ( $n = 25$ ) who received HDR brachytherapy treatment at a hospital in Montreal, Quebec, completed verbal analog scales for pain and anxiety at 4 time points over 4 treatment days.

### Results

On all 4 days, a subset of patients reported moderate-to-severe anxiety before applicator insertion. Pain increased significantly from the time patients were lying on the table to immediately after insertion of the applicator ( $p < 0.001$ ). Insertion of the applicator appears to be the most painful part of the procedure, and although anxiety declined to below baseline after applicator removal, pain remained somewhat elevated. Some patients required conscious sedation; however, reports of moderate-to-severe pain were more frequent from patients who received pain medications than from patients who did not receive such medication ( $p < 0.05$ ).

### Conclusions

Most patients with rectal cancer tolerated HDR rectal brachytherapy well, although the procedure is stress-

ful and painful for some. Insertion of the applicator was found to be the point of maximal pain, and medication was not always completely successful at alleviating the pain, suggesting that additional psychosocial interventions might be needed, with particular emphasis on the time of applicator insertion.

## KEY WORDS

Brachytherapy, rectal cancer, procedural pain, anxiety, psycho-oncology, patient experience, cancer treatment

## 1. INTRODUCTION

In the treatment of rectal cancer, intracavitary high dose rate (HDR) brachytherapy is an important treatment modality, which has been innovated at our outpatient radiation oncology clinic at the Jewish General Hospital in Montreal, Quebec. One widely acknowledged advantage of HDR brachytherapy over external-beam radiation therapy is that, compared with radiation therapy, HDR brachytherapy has a considerably shorter duration and targets the tumour more focally, resulting in better sparing of normal tissues. At the same time, HDR brachytherapy presents physicians with numerous challenges. First, it can be extremely painful, and it thus requires both analgesia and immobilization. Second, the duration of an HDR brachytherapy procedure is highly variable. Multiple sessions are frequently required, and during serial treatments, repeated analgesia might be necessary.

Recent studies have explored the pain and anxiety experience during brachytherapy, primarily in women's cancers (cervical, breast) and in prostate cancer<sup>1</sup>. Overall, the literature suggests that, although the treatment is relatively well-tolerated by most patients, a small proportion experience significant pain and anxiety<sup>2</sup>. Little is known about the degree and intensity of the pain and anxiety experienced by patients undergoing HDR brachytherapy for rectal cancer. Studies of colorectal cancer patients have shown that they experience a high prevalence of

anxiety, depression, and treatment-related distress<sup>3,4</sup>. Currently, there is no consensus on the most effective analgesia for HDR rectal brachytherapy.

The purpose of the present study was to describe the pain and anxiety experience of rectal cancer patients during a course of HDR brachytherapy. We also aimed to gather empiric evidence about the trajectory of pain and anxiety symptoms and the point of maximal symptom intensity. Ultimately, the goal was to better understand the patient experience so as to conduct future studies assessing psychosocial interventions that might help to reduce pain and anxiety for the patient during HDR brachytherapy.

## 2. METHODS

### 2.1 Participants

Our study included 26 patients with stage I, II, or III rectal cancer. All patients were undergoing HDR brachytherapy as part of their cancer treatment at the Jewish General Hospital outpatient radiation oncology clinic. All patients were more than 18 years of age, had pathology-confirmed rectal cancer and gave informed consent to participate in the study. Patients were excluded if they showed cognitive impairments, as evidenced by a score of 24 or less on the Mini-Mental State Examination, or if they had a psychiatric diagnosis currently being treated with medication (per medical chart review). No patients had to be excluded based on those criteria. The brachytherapy treatment logistics and protocol and the research study were explained in detail to all patients. The study was approved by the Ethics Review Committee of the Jewish General Hospital and was conducted according to institutional guidelines.

### 2.2 HDR Brachytherapy Treatment

Patients were treated on an outpatient basis with 4 daily fractions of 6.5 Gy (1 fraction per day for 4 days, with the potential for a day of rest between treatment days, depending on clinic scheduling) per the institution's standard protocol for HDR brachytherapy treatment. Typically, each HDR brachytherapy treatment takes approximately 1.5 hours, but can last up to 2.5 hours.

Patients were escorted to the treatment room and assisted to the computed tomography (CT) stimulator table in lithotomy position (legs in stirrups). Standard topical analgesia with lidocaine gel was applied per hospital protocol. Once an adequate level of analgesia was achieved, the attending physician performed a digital rectal examination (DRE). If patients reported pain during the DRE, they were offered medication: midazolam 1–2 mg and fentanyl 100–150 µg given intravenously. Lidocaine gel was reapplied. The attending physician then inserted the applicator into the rectum. While the patient remained immobile, with the applicator fixed in the rectum, three-dimensional

CT imaging was performed for planning, and the dose was calculated<sup>5,6</sup>. The source of HDR radiation was then attached to the patient, and localized radiation was administered. After the HDR brachytherapy had been delivered, the applicator was removed, and the patient was assisted off the treatment table. This procedure was repeated on each of the 4 treatment days.

### 2.3 Measures

Since the early 2000s, a verbal analog scale (VAS) has been used in several interventional radiology procedures to assess pain and anxiety<sup>2,7–10</sup>. Additionally, the use of a VAS was reported in various groups of patients receiving consciously sedation or no sedation and was found to be reliable<sup>11,12</sup>. The VAS, which uses a discrete 10-point scale ranging from 0 (no pain or no anxiety) to 10 (worst possible pain or worst possible anxiety), has demonstrated external validity and sufficient sensitivity in measuring symptom levels. It has been recommended for use in medical settings in which written self-report is not possible<sup>10</sup>.

### 2.4 Procedure

The attending radiation oncology technologist asked patients to use the VAS to rate their pain and anxiety at 4 time points:

- Time A: When the patient first reclined on the treatment table
- Time B: Immediately after insertion of the applicator
- Time C: Just before initiation of HDR treatment delivery
- Time D: Immediately after removal of the applicator

The CT imaging, dose calculations, and planning occurred between time points B and C.

### 2.5 Statistical Analyses

The variables collected from patients or their medical charts were sex, language, relationship status, occupation, alcohol consumption, smoking status, cancer stage, functional status, family history of cancer, and use of analgesic medication during HDR brachytherapy.

The primary outcome variables were the VAS pain and anxiety scores. Means (with standard deviation) and percentages are reported to describe the central tendency and dispersion of scores. The raw scores were then grouped into two categories: 0–3, mild symptoms; 4 or more, moderate-to-severe symptoms. The moderate and severe categories are combined because patients in both categories would likely require an intervention. These categories of severity scoring have been used in similar research and are used to classify symptom intensity into specific categories to

help guide treatment decisions. The Wilcoxon signed-rank test was used to identify whether the population mean rank differed for time A compared with the point of maximal score for pain and anxiety. The Fisher exact test was used to examine the association between pain and use of pain medication. Univariate analysis of variance used to explore correlations and relations between anxiety and pain. A  $p$  value of 0.05 or less (two-tailed  $t$ ) was considered statistically significant. All analyses were conducted using the PASW Statistics software application (version 18.0, SPSS, Chicago, IL, U.S.A.).

### 3. RESULTS

From April 2010 to January 2011, 26 patients consented to the study and met the eligibility criteria. One patient switched to external-beam radiation therapy and was excluded from the analysis, leaving a sample of 25 patients (mean age:  $61 \pm 11$  years). Table I summarizes patient demographics and disease characteristics.

#### 3.1 Anxiety VAS

Table II summarizes the mean scores on each day's anxiety VAS at times A, B, C, and D. On day 1, when the patient was reclined on the treatment table and the applicator was not yet inserted (time A), 7 of 25 patients (28%) reported moderate or severe anxiety (score  $\geq 4$ , Figure 1). Immediately after insertion of the applicator, the percentage of patients reporting moderate or severe anxiety significantly increased to 44% ( $p = 0.021$ ) and remained elevated at 36% during HDR treatment delivery. Immediately after removal of the applicator, anxiety declined significantly to 12% ( $p < 0.03$  compared with time A).

On subsequent procedure days, the proportion of patients reporting moderate or severe anxiety after insertion of the applicator and before HDR treatment delivery (times B and C respectively) was lower than it had been on day 1 (Figure 1). Additionally, no significant increase in anxiety compared with anxiety at time A ( $p > 0.1$ ) was observed after insertion of the applicator for any of days 2, 3, or 4. However, the proportion of patients reporting moderate or severe anxiety before insertion of the applicator remained elevated on subsequent days, as on day 1. Anxiety seems to decline by the end of the procedure, because very few patients reported moderate or severe anxiety after removal of the applicator (time D).

#### 3.2 Pain VAS

Table II summarizes mean scores on the pain VAS for each day at times A, B, C, and D. On day 1, before insertion of the applicator, all 25 patients were free of moderate or severe pain. After insertion of applicator, 9 of 25 patients (36%) reported moderate or severe pain (score  $\geq 4$ , Figure 2). The proportion of patients

TABLE I Patient characteristics

Characteristic	Value [n (%)]
Sex	
Men	20 (80)
Women	5 (20)
Language	
French	19 (76)
English	6 (24)
Relationship status	
Married	13 (52)
Widowed	1 (4)
Separated	2 (8)
Occupation	
Employed	9 (36)
Retired	12 (48)
Smoking status	
<1 Pack daily	6 (24)
>1 Pack daily	1 (4)
Former smoker	10 (40)
Nonsmoker	8 (32)
Cancer stage	
I	2 (8)
II	11 (44)
III	12 (48)
ECOG performance status <sup>a</sup>	
0	15 (60)
1	10 (40)
Family history	
CRC or rectal polyps only	2 (8)
Other cancers only	13 (52)
CRC and other cancers	5 (20)
None	4 (16)

<sup>a</sup> A score of 0 denotes a patient who is fully active; a score of 1 denotes a patient who is restricted in physically strenuous activity, but who is ambulatory and can do light work.

ECOG = Eastern Cooperative Oncology Group; CRC = colorectal cancer.

reporting moderate or severe pain remained high during HDR treatment delivery and declined slightly after removal of the applicator. The difference in the percentage of patients reporting moderate or severe pain between time A and times B, C, and D was statistically significant ( $p < 0.001$ ).

The trajectory of the pain on subsequent procedure days remained similar to that on day 1. Compared with the proportion of patients reporting moderate or severe pain at time A, the proportion reporting moderate or severe pain was significantly higher on every subsequent day, at every subsequent point during the procedure (that is, at times B, C, and D;  $p < 0.001$ ; Figure 2). Notably, on days 2, 3, and

4, 8%–12% reported moderate or severe pain before applicator insertion, which contrasts with the 0% reported on day 1.

The percentage of patients reporting moderate or severe pain was highest at insertion of the applicator (days 1, 2, and 4), with 20%–45% of patients reporting moderate or severe pain immediately after insertion. For most patients, that moderate or severe pain remained during treatment delivery and even after removal of the applicator.

At any given time point, anxiety and pain were significantly correlated ( $p < 0.01$ ). Univariate analysis of variance showed that 20% of anxiety might be related to pain ( $R^2 = 0.22$ ).

The number of patients requesting conscious sedation increased from 3 of 25 (12%) on day 1 to 8 of 25 (32%) on day 4 (Figure 3). On all 4 days, moderate or severe pain was reported more frequently by

patients who received pain medication than by those who did not ( $p < 0.05$ , Figure 4).

#### 4. DISCUSSION

In the present study, we examined patient reports of pain and anxiety during HDR brachytherapy with standard local analgesia. To our knowledge, our study is the first to examine pain and anxiety trajectories in rectal cancer patients undergoing HDR brachytherapy. Although treatment was relatively well tolerated by most patients under local anesthesia, more than 30% experienced moderate or severe anxiety and pain that was not alleviated by standard pain medications. The highest percentage of moderate or severe pain was reported at insertion of the applicator, which suggests that insertion is the most painful moment during HDR brachytherapy.

We cannot compare our findings with those in the same population by other investigators because no other reports have been published to date. However, our results accord with findings from a study of cervical cancer patients undergoing HDR brachytherapy, in which 29% of participants reported moderate to severe distress (score  $\geq 4$ ).<sup>2</sup>

In our study, the initial treatment day appeared to be the most anxiety-provoking, particularly after insertion of the applicator. The trajectory of anxiety remained similar on subsequent procedure days, such that patients reported moderate or severe anxiety before insertion, but that anxiety declined over subsequent procedure days. In other words, by the time the applicator was removed, the report of moderate or severe anxiety was low. However, anxiety remained elevated at onset of the procedure (time A) on each new treatment day. That result directly contrasts with the findings in the cervical cancer patients undergoing HDR brachytherapy, who reported lower distress ratings during subsequent procedures<sup>2</sup>. In our population, familiarity with procedure did nothing to reduce anxiety levels. Accommodation with multiple exposures seemed not to occur; each session had its own associated anxiety, possibly because of the anticipatory anxiety that patients feel on each day of treatment, knowing that the applicator will soon be inserted.

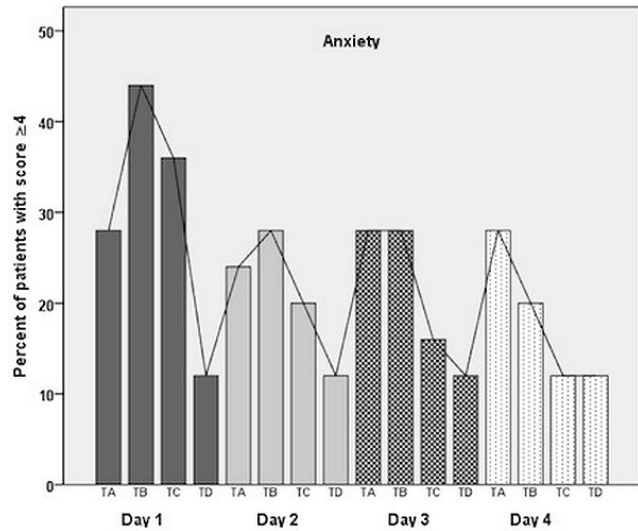


FIGURE 1 Anxiety scores during high dose rate (HDR) brachytherapy over 4 treatment days. Bars represent the number of patients whose verbal analog anxiety scores reached 4 or higher. The solid line tracks the overall anxiety trajectory. Anxiety increased significantly from time A (TA) to time B (TB) on day 1 ( $p < 0.001$ ). TA = patient reclines on the treatment table; TB = immediately after insertion of the applicator; TC = time C, just before initiation of HDR treatment delivery; TD = time D, immediately after removal of the applicator.

TABLE II Mean verbal analog scores for anxiety and pain during high dose rate brachytherapy

Time point	Anxiety				Pain			
	Day 1	Day 2	Day 3	Day 4	Day 1	Day 2	Day 3	Day 4
TA	2.6±2.2	2.1±2.4	2.6±2.7	2.0±2.3	0.3±0.8	0.9±1.7	1.1±2.1	0.9±2.0
TB	3.1±2.1	2.4±2.6	2.9±2.7	2.6±2.4	2.9±2.3	3.4±2.8	3.2±2.6	3.5±2.6
TC	2.9±2.3	1.9±2.3	1.7±2.1	1.7±1.5	2.9±2.4	3.0±2.3	3.0±2.2	3.0±2.5
TD	1.4±1.7	1.4±1.9	1.3±1.5	1.5±1.5	2.6±1.7	2.7±2.2	2.7±2.2	2.8±2.3

TA = time A, patient reclines on the treatment table; TB = time B, immediately after insertion of the applicator; TC = time C, just before initiation of HDR treatment delivery; TD = time D, immediately after removal of the applicator.



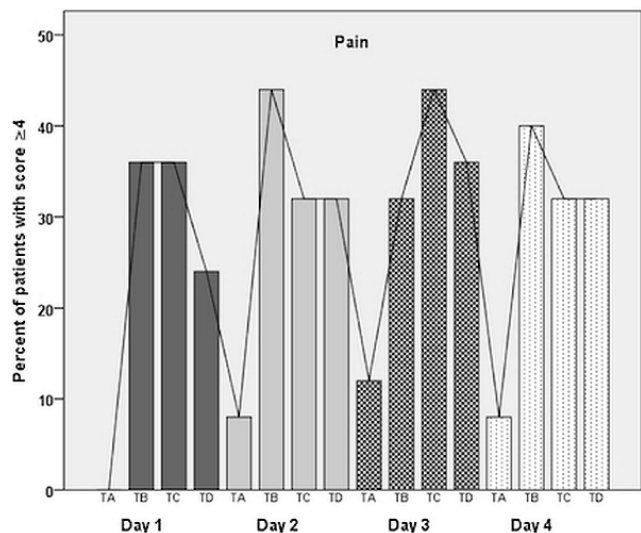


FIGURE 2 Pain scores during high dose rate (HDR) brachytherapy over 4 treatment days. Bars represent the number of patients whose verbal analog pain scores reached 4 or higher. The solid line tracks the overall pain trajectory. Pain increased significantly from time A (TA) to time B (TB) on all 4 days ( $p < 0.001$ ). Pain remained significantly high at time C (TC) and time D (TD) compared with TA on all 4 days ( $p < 0.001$ ). TA = patient reclines on the treatment table; TB = immediately after insertion of the applicator; TC = just before initiation of HDR treatment delivery; TD = immediately after removal of the applicator.

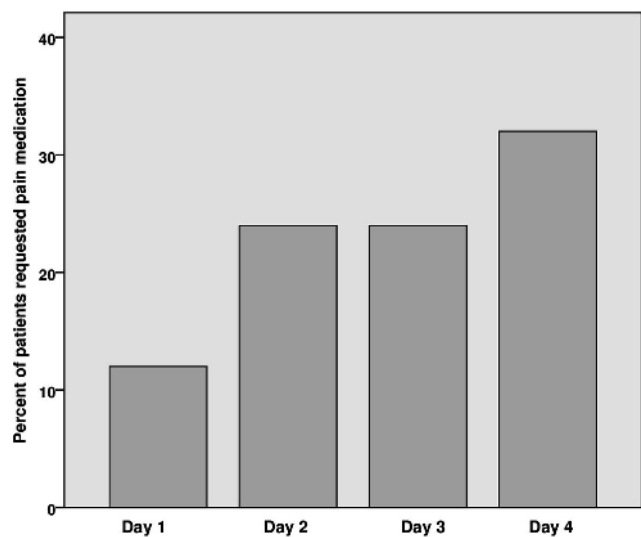


FIGURE 3 Number of patients requesting analgesic medication after the digital rectal exam during 4 treatment days.

There is no agreement on the point of maximal physical and emotional distress in various cancer populations undergoing brachytherapy. Kwekkeboom and colleagues<sup>2</sup> reported that, in cervical cancer patients undergoing brachytherapy, the highest pain was observed at removal of the applicator. The authors suggest that this finding might be related to the effects of conscious sedation having

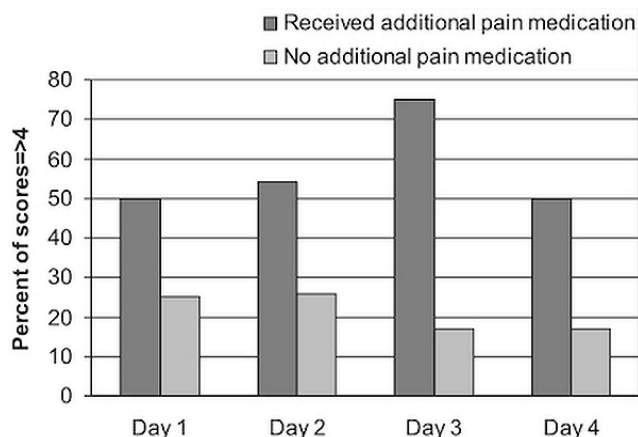


FIGURE 4 Compared with patients who took no pain medication during the procedure, those who took pain medication more frequently reported a moderate or severe level of pain.

possibly worn off by the end of treatment<sup>2</sup>. A study of assorted gynecologic cancer patients found that pain was highest after transfer to the CT scanner ( $\mu = 3.3$ )<sup>13</sup>. In our population of rectal cancer patients, it appears that the point of maximal pain occurred immediately after insertion of the applicator. That result suggests the importance of tailoring analgesia protocols to the given type of brachytherapy when treating a specific cancer.

Sedation, often with fentanyl and midazolam, although not strictly speaking an analgesic technique, is frequently used in HDR brachytherapy in addition to local analgesia (lidocaine gel). The lack of an effective marker for the prediction of pain prevents us from determining ahead of time which patient group needs conscious sedation. We used DRE as a pain marker, and 24% of the patients who reported pain during the DRE were given conscious sedation. Despite receiving analgesic medication, most of those patients still experienced moderate to severe pain throughout the procedure. Interestingly, moderate or severe pain was reported more frequently by patients who received pain medication than by those who did not.

Anxiety and pain were significantly correlated. However, pain contributed to only 20% of the anxiety. Other unknown factors that might be influencing anxiety have to be explored. Cancer pain is known to be a multidimensional construct consisting of sensory and emotional components, with the emotional component of pain above the sensory<sup>14</sup>. It might be speculated that analgesic medications alleviate sensory pain, leaving the elevated emotional pain. Thus, the emotional component of pain might require a different type of treatment for pain management.

Of cervical cancer patients treated with brachytherapy, 26% still experienced severe uterine pain even with conscious sedation<sup>2</sup>. Pharmacologic treatments are the central component of cancer pain management, but the absence of adequate anesthesia

during brachytherapy can cause tremendous pain. That experience might lead to physiologic and psychological changes that contribute to the development of chronic pain, poor compliance, and poor quality of life, and that interfere with a sequential treatment protocol. A 2012 meta-analysis of 37 studies showed moderate-to-large pain-relieving effects from hypnosis, supporting the effectiveness of hypnotic techniques for pain management in cancer patients<sup>15</sup>. We postulate that psychosocial interventions—including hypnosis, meditation, and relaxation—when added to pharmacologic intervention may help to alleviate pain during HDR brachytherapy.

Our study has several limitations. The study enrolled a relatively small number of patients from a single institution. Results from this single-institution group might not be generalizable to other populations. Our sample was composed predominately of men, and future studies might want to consider the influence of sex on pain and anxiety. As with any study, use of self-reported subjective experience might introduce some bias, because results might be influenced by a variety of factors, including patient discomfort, social and cultural factors, and individual differences in pain tolerance, among others. Moreover, our study was not specifically designed to evaluate the level of anxiety before initiation of the procedure. Future studies should consider obtaining baseline anxiety scores (for example, at home on the day before treatment), which might be informative in this patient population.

## 5. CONCLUSIONS

For most patients with rectal cancer, HDR brachytherapy is a well-tolerated procedure. However, it is anxiety-provoking and painful for at least some recipients, despite additional pharmacologic intervention. Notably, insertion of the applicator was found to be the point of greatest pain.

Taken together, our findings suggest that there are unmet needs in patients experiencing anxiety and pain during HDR brachytherapy for rectal cancer. It could be of great clinical utility to educate the health care team about the times that patients experience peak pain and anxiety, so that the team can work together to better the experiences of colorectal cancer patients, at least during the narrow experience of treatment. Future research should explore the characteristics of patients who might be at risk for pain or anxiety during HDR brachytherapy and consider offering management alternatives, possibly including nonpharmacologic pain control in addition to a pre-emptive analgesia protocol. The nonpharmacologic direction of research in this area might begin by exploring psychosocial interventions (for example, relaxation or hypnosis). It might also be appropriate to consider implementing such psychosocial interventions before maximum pain is encountered—in other words, before insertion of the applicator.

## 6. ACKNOWLEDGMENTS

This research was supported by the Ride to Conquer Cancer and the Jewish General Hospital Foundation. We acknowledge the contributions of the Jewish General Hospital's Radiation Oncology brachytherapy staff and technologists: Catherine Laganier, Julie De Cristofaro, Rita Kassalti, and Toan Vo. We also thank Isabel Dao and Tamara Greenidge, and acknowledge the time and efforts of Goulnar Kasymjanova and Leonora King.

## 7. CONFLICT OF INTEREST DISCLOSURES

The authors have no financial conflicts of interest to declare.

## 8. REFERENCES

1. Hruby G, Chen JY, Bucci J, Loadman JA, Perry P, Stockler MR. Patients' experiences of high-dose rate brachytherapy boost for prostate cancer using an inpatient protocol. *Brachytherapy* 2011;10:395–400.
2. Kwekkeboom KL, Dendaas NR, Straub M, Bradley KA. Patterns of pain and distress during high-dose-rate intracavity brachytherapy for cervical cancer. *J Support Oncol* 2009;7:108–14.
3. Tsunoda A, Nakao K, Hiratsuka K, Yasuda N, Shibusawa M, Kusano M. Anxiety, depression and quality of life in colorectal cancer patients. *Int J Clin Oncol* 2005;10:411–17.
4. Sehlen S, Hollenhorst H, Schymura B, *et al.* Psychosocial stress in cancer patients during and after radiotherapy. *Strahlenther Onkol* 2003;179:175–80.
5. Vuong T, Devic S, Moftah B, Evans M, Podgorsak EB. High-dose-rate endorectal brachytherapy in the treatment of locally advanced rectal carcinoma: technical aspects. *Brachytherapy* 2005;4:230–5.
6. Vuong T, Richard C, Niazi T, *et al.* High dose rate endorectal brachytherapy for patients with curable rectal cancer. *Semin Colon Rectal Surg* 2010;21:115–19.
7. Lang EV, Berbaum KS, Faintuch S, *et al.* Adjunctive self-hypnotic relaxation for outpatient medical procedures: a prospective randomized trial with women undergoing large core breast biopsy. *Pain* 2006;126:155–64.
8. Benotsch E, Lutgendorf S, Watson D, Fick L, Lang E. Rapid anxiety assessment in medical patients: evidence for the validity of verbal anxiety ratings. *Ann Behav Med* 2000;22:199–203.
9. Montgomery GH, Weltz CR, Seltz M, Bovbjerg DH. Brief presurgery hypnosis reduces distress and pain in excisional breast biopsy patients. *Int J Clin Exp Hypn* 2002;50:17–32.
10. Schupp CJ, Berbaum K, Berbaum M, Lang EV. Pain and anxiety during interventional radiologic procedures: effect of patients' state anxiety at baseline and modulation by nonpharmacologic analgesia adjuncts. *J Vasc Interv Radiol* 2005;16:1585–92.
11. Ni YL, Lo YL, Lin TY, Fang YF, Kuo HP. Conscious sedation reduces patient discomfort and improves satisfaction in flexible bronchoscopy. *Chang Gung Med J* 2010;33:443–52.
12. Ahlers SJ, van der Veen AM, van Dijk M, Tibboel D, Knibbe CA. The use of the Behavioral Pain Scale to assess pain in conscious sedated patients. *Anesth Analg* 2010;110:127–33.

13. Wiebe E, Surry K, Derrah L, *et al.* Pain and symptom assessment during multiple fractions of gynecologic high-dose-rate brachytherapy. *Brachytherapy* 2011;10:352–6.
14. Sela RA, Bruera E, Conner–Spady B, Cumming C, Walker C. Sensory and affective dimensions of advanced cancer pain. *Psychooncology* 2002;11:23–34.
15. Sheinfeld Gorin S, Krebs P, Badr H, *et al.* Meta-analysis of psychosocial interventions to reduce pain in patients with cancer. *J Clin Oncol* 2012;30:539–47.

**Correspondence to:** Sylvain Néron, Segal Cancer Centre, Jewish General Hospital 3755 Chemin de la Côte-Sainte-Catherine, Room E-755, Montreal, Quebec H3T 1E2.

**E-mail:** sylvain.neron@mcgill.ca

- \* Louise-Granofsky Psychosocial Oncology Program, Segal Cancer Centre, and Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, QC.
- † Psychology Department, McGill University, and Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, QC.
- ‡ Segal Cancer Centre, Jewish General Hospital, Montreal, QC.
- § Segal Cancer Centre and Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, QC.