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Radiation Therapy and Pain in Patients with Head and Neck Cancer

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Pain is commonly present at the time of diagnosis of head and neck cancer. Pain occurs in all patients treated for oropharyngeal cancer. This study examined the prevalence, severity and characteristics of pain in patients treated with radiation therapy for cancer involving the head and neck and oral cavity. Pain increases throughout the course of radiation and persists following treatment and in some patients continues for 6–12 months. Pain frequently requires systemic analgesics in addition to oral rinses.
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PAIN DUE to cancer therapy is common and can represent either direct toxicity or delayed complications of therapy [1–9]. Pain is influenced by emotional, social, ethnic, environmental and financial considerations [1, 5–16]. Pain as a result of cancer has important psychological components [3, 4, 6, 7, 16–25]. Anxiety, fear and depression increase the experience of pain. The patient with oral and maxillofacial cancer and complications from treatment is especially unique because body image can be significantly affected. Pain, whether related or unrelated to cancer, often produces fear of progression of the disease which may heighten the experience of pain [1, 4, 16, 20].

Acute pain following cancer surgery is an obvious complication of treatment. In addition, surgery may result in damage to neural structures that may lead to persistent neuropathic pain [5, 6, 26–28]. Deafferentation has been shown to result in change in the receptive field of neurons, development of spontaneous neuron activity, and reduction in central control mechanisms that may result in neuropathic pain [29–32]. Pain may also develop due to loss of function of the jaw following surgical resection, discontinuity of the jaw and fibrosis of tissue leading to altered function.

The incidence and severity of pain increases during radiotherapy for treatment of cancer of the head and neck [1, 33, 34]. Radiotherapy-related pain results from direct damage to normal tissues due to epithelial thinning, mucosal atrophy, inflammation and ulceration [1, 35–38]. Mucositis may be worsened by xerostomia because of the loss of lubrication of tissues, dehydration of the mucosa and due to secondary infection of the mucosa. The severity and onset of mucositis is directly related to the dose and frequency of radiation therapy. However, there are marked individual variations.

There is limited information on the incidence, severity and description of orofacial/oropharyngeal pain in cancer patients. Self reporting of pain using questionnaires (i.e. McGill pain questionnaire), visual analogue scales, verbal rating scales, pain behaviours, reports of pain severity and medication use, have been used in few studies in cancer patients [26, 33, 39]. Only one study has evaluated head and neck pain [33]. There is a dramatic need to assess the efficacy of pain control and quality of life in patients with cancer of the head and neck [25]. The purpose of this study was to develop a pain questionnaire applicable to head and neck and oral pain in cancer patients. The questionnaire explored the incidence, severity and duration of pain, and the effects of topical and systemic treatment of the pain.

PATIENTS AND METHODS

Patients planned to receive radiation therapy for head and neck or oropharyngeal cancers were included in the survey. All patients had a complete head and neck, oral and dental examination, screening panoramic radiographs and selected dental periapical radiographs. Teeth with moderate to severe periodontal disease that would be within the high dose radiation treatment volume were extracted. Teeth with symptomatic periapical pathosis were treated with pulpectomy or extraction. Additional dental treatment provided for dentate patients was dental prophylaxis, oral hygiene instruction, and daily fluoride applied by the patient with the use of neutral fluoride gel in custom carriers.

The questionnaire incorporated visual analogue scales (VAS) for pain, recording of medications used, the efficacy of medications, anatomical diagrams to allow graphical representation of pain location, descriptors of pain, and a portion of the McGill pain questionnaire. Patients were provided the self-administered questionnaire following the pre-radiotherapy oral and dental assessment, at the mid-point of radiotherapy, at the end of radiation therapy, at 1 month follow-up and between 6 and 12 months following treatment. If patients did not complete the questionnaire at the clinic the questionnaire was mailed to the patient for completion. Staff were available to answer any patient questions. The questionnaire was developed and pretested prior to its clinical use. The responses to the questionnaire were entered into D-base III plus for review.

RESULTS

34 patients who received radical radiotherapy that included the oral cavity participated in the survey. The mean age was 63 years (range 41–86 years). There were 26 males and 15 females.

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Table 1. Tumour site and staging of oral squamous cell carcinoma

Site	(n)	Primary tumour	(n)	Lymph node involvement	(n)	Metastases	(n)
Lip	5						
Tongue	8	T1	4	N0	21	M0	33
Cheek	2	T2	14	N1	10	M1	1
Palate	1	T3	13	N2	1		
Floor of mouth	4	T4	3	N3	2		
Pharynx/tonsil	12						
Sinus	2						

Of the 34 patients, 31 had a diagnosis of squamous cell carcinoma (SCC) and 3 had malignant salivary gland tumours. Tumour staging of the SCC is shown in Table 1. Alcohol consumption and smoking history is shown in Table 2.

In 13 patients external beam radiation therapy was provided to a total dose of 5000 cGy in 20 fractions, and in 21 patients to 6000 cGy in 25 fractions. 5 patients had received surgical resection of tumour prior to radiotherapy, these included 3 patients with bone involvement (T4) treated with combined surgical resection and radiation, and 2 other patients who had primary tumour resection with positive margins requiring post-operative radiotherapy. Acute surgical pain had resolved prior to radiotherapy which was initiated 6 to 15 weeks following surgery. All other patients were treated with primary radiation therapy. 4 patients required surgery following radiotherapy, 3 of these received radical neck dissection due to lymph node involvement, and 1 required surgical treatment for persisting disease.

The results of the pain survey are shown in Table 3. Pain was present at the time of diagnosis in 82%. The initial level of pain was low with a mean VAS of 23. The site of pain was identified as involving the oral cavity in 19 patients, and in the head and neck in 9. The mean duration of pain prior to diagnosis was 3.6 months. Pain for less than 1 month was reported by 1 patient. The majority experienced pain from 1 to 3 months (12 patients) and 3 to 6 months (14 patients). Pain for more than 6 months was reported by 1 patient. Pain was described as mild by the majority of patients. Analgesics were used before radiation therapy by 15 patients, these included 2 non-narcotic analgesics, 11 narcotic-non-narcotic analgesics (e.g. acetominophen or acetylsalicylic acid and codeine), and 2 required potent oral narcotics (e.g. leritine, morphine).

Table 2. Alcohol and smoking history

Type of alcohol		Frequency of consumption	
None	3	Weekly	5
Beer	7	1–2 WE/day	9
Wine	4	2–6 WE/day	10
Hard spirits	12	>6 WE/day	5
Combination	6		
Missing	2		
Smoking cigarettes	None	2	
	<20/day	4	
	<40/day	10	
	>40/day	12	
	Missing	6	

WE = whiskey equivalent; 1 = 1 beer or 1 oz liquor.

By the midpoint of treatment all 34 patients experienced pain, with a mean VAS of 38 mm. In 82% pain involved the oral cavity. The description of pain was mild in 10, distressing in 17 and horrible in 7. Pain was managed with systemic medications in 69% and oral rinses in 85%. No patients had been prescribed psychoactive agents or sedative agents.

30 patients were reviewed at the end of treatment and all but 1 patient reported pain. The mean VAS level was 45 mm. Pain was described as mild in 10, distressing in 15 and horrible in 8. The pain was continuous in 17, periodic and intermittent in 8 and brief or transient in 4. Systemic analgesics were provided in 93% of patients. 2 patients were prescribed benzodiazepines. Oral rinses were used by 90% of patients.

27 patients were reviewed 1 month following radiation therapy. 16 patients continued to experience pain. The mean VAS pain score was 19 mm. Pain was described as mild in 11 and distressing in 5. Medications used at that time were systemic analgesics in 11 patients, and oral rinses in 18.

The final pain assessment was conducted from 6–12 months following radiation treatment in 26 patients. 12 patients continued to experience pain. Pain was present in the head and neck in 8, orally in 1, and at sites not identified in 3 patients. The mean VAS was 18 mm. Pain was described as mild in 9 and distressing in 2. Systemic analgesics were used in 23% of patients evaluated. Oral rinses were continued by 19%. Resolution of pain was described as unlikely in 2, likely in 3 and uncertain in 3.

DISCUSSION

Discomfort is the primary reason patients seek treatment and has been reported in up to 85% of patients [4, 33–35, 40–44]. In this study, 82% of patients reported discomfort at diagnosis. Alteration of the surface epithelium, loss of the normal barrier function, exposure of nerves, direct tumour effects on nerve function or invasion or chemosensitisation of receptors, and secondary infection of the lesion appear to be the aetiology of pain [6, 45–49]. Pain predated diagnosis by a mean of 3.6 months and the majority experienced discomfort for 1 to 6 months, indicating a delay in presentation and/or delay in diagnosis.

Pain at diagnosis is of low to moderate intensity, and generally described as discomfort [27, 33, 34, 41, 50–52]. Pain was described as mild in the majority of patients and scored as 23 (range 0–80) by VAS. Disease stage and site and pretreatment pain has been reported to predict pain at the end of treatment (33, 431). In this survey pain was related to tumour size (Fig. 1). No relation between pain and smoking or alcohol consumption was seen.

In all cases with radiographic evidence of bone involvement pain was reported. This is similar to past literature where pain was associated with bone involvement in 85% of body sites [4]. While pain is related to tumour size, therapy related pain is reported as the predominant cause of pain [41]. In our survey all patients reported pain during treatment, with increasing severity throughout radiotherapy (Figs 2 and 3).

The initial analgesic selected should be the least potent analgesic that relieves the pain, when needed narcotic agents should be used in combination with non-narcotics [4, 5, 19, 23, 35, 53, 54]. Analgesics should also be used on a time contingent basis [4, 5, 9, 14, 19, 20, 22, 23, 53–63]. A major problem in analgesic use in cancer patients is the reluctance of health-care workers to provide adequate doses and frequency of medication to effectively control the pain, in spite

Table 3. Progress of pain throughout the course of radiotherapy

No. of patients	Visit 1 % ($n=34$)	Visit 2 % ($n=34$)	Visit 3 % ($n=30$)	Visit 4 % ($n=27$)	Visit 5 % ($n=26$)
Presence of pain	82 (28)	100 (34)	97 (29)	59 (16)	46 (12)
Pain (VAS)					
Mean	23	38	45	19	18
Range	0–80	5–85	0–100	0–70	0–50
Site of pain					
Oral	17	20	17	9	1
Head and neck	9	4	5	3	8
Both	2	8	7	4	—
Missing data	3	2	—	—	3
Description					
None	6	0	1	11	14
Mild	17	10	7	11	9
Distressing	9	17	15	5	2
Horrible	—	7	7	—	—
Missing data	2	—	—	—	1
Pain duration					
Continuous	9	15	17	6	5
Intermittent	12	14	8	6	3
Brief	7	5	4	4	4
Missing data	2	—	—	—	—
Analgesics					
Non-narcotic	2	4	4	3	2
Mild narcotic	11	16	16	6	2
Narcotic	2	5	8	2	2
Oral rinses					
Benzydamine	—	16	20	18	4
Xylocaine	—	13	7	2	1
Baking soda	—	3	4	5	3
Missing data	—	1	—	—	—
Pain resolution					
Certain	—	—	—	8	—
Likely	—	—	—	3	3
Uncertain	—	—	—	2	3
Unlikely	—	—	—	1	2
Impossible	—	—	—	1	1

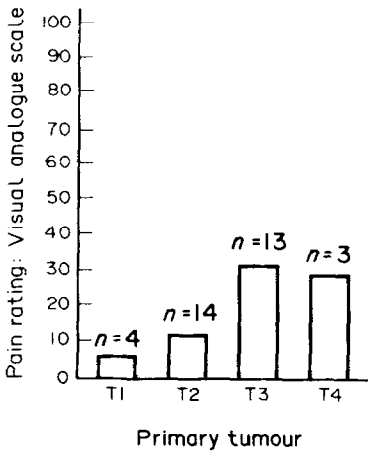

Fig. 1. Pain at diagnosis and tumour size.

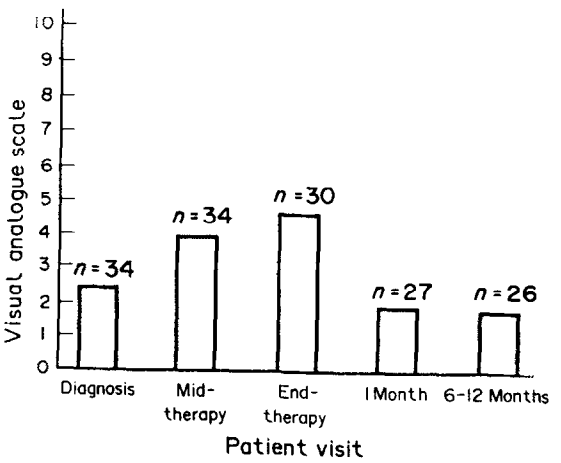

Fig. 2. Oropharyngeal pain experience during radiation therapy.

of evidence that use of narcotics in cancer patients with pain does not result in addiction [4, 5, 7, 41, 44, 53, 56, 64–70]. The evidence of universal increased pain in the survey indicates increasing pain in spite of oral rinses and systemic analgesics and indicates the need for improved pain control.

Pain relief is well documented in cancer patients with the use of psychotropic medications [4, 7, 18, 45, 53, 59, 61, 71–78]. The psychotropic drugs may act synergistically with other analgesic drugs by analgesic effects due to different mechanisms of action, improving sleep, and by altering the emotional state of the patient [79–83]. Side effects of sedation, fluid retention, and dry mouth are generally better tolerated at analgesic doses, however, elderly patients appear to be more

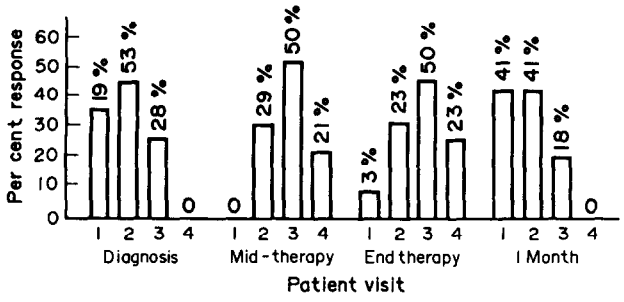

Fig. 3. Pain description during radiation therapy. Key: 1 = none; 2 = mild; 3 = distressing; 4 = horrible.

susceptible. In spite of abundant data on the efficacy of tricyclics in pain, including pain in cancer patients, there were no prescriptions of tricyclics in the patients in this survey.

Anti-anxiety agents, including the benzodiazepines, may reduce anxiety and act as adjuvants in muscular pain [5, 7, 84]. Steroids reduce inflammation and oedema that may be associated with malignant conditions, and may therefore reduce pain [5]. These drugs may also affect mood, and improve appetite [5, 85]. In 2 patients in the survey benzodiazepines were used during the course of their care.

Mucositis pain is managed palliatively until healing occurs. Bland rinses (0.9% saline solutions with or without sodium bicarbonate), topical anaesthetics, and mucosal coating agents have been suggested but have not been subjected to double blind studies [34, 35, 38, 86–88]. Lidocaine viscous is frequently recommended on clinical grounds. However, the rinse may result in burning sensation when mucosal ulcers are present and may eliminate the taste sensation affecting dietary intake. Topical lidocaine may cause cardiovascular and CNS toxicity (seizures) and the degree of anaesthesia may cause loss of the gag reflex increasing the risk of aspiration [34, 89, 90]. Clinical trials using benzydamine, a topical non-steroidal anti-inflammatory agent to treat the pain of oral mucositis, and to prevent mucositis have shown encouraging results [34, 91, 92]. Benzydamine produces topical analgesia and mild anaesthesia, and may reduce mucosal breakdown due to stabilisation of cell membranes [92, 93]. Topical analgesics and anaesthetics may be helpful when they are applied to localised areas or used as a rinse when mucosal involvement is widespread. Systemic agents may be needed in addition to topical anaesthetic or analgesic agents. Due to the efficacy of benzydamine in controlled clinical trials at our institution, it has become the first choice in topical therapy.

Musculoskeletal syndromes are commonly seen in patients with cancer. The aetiology of dysfunction includes direct effects of the tumour in muscles that may limit mandibular movement, bone destruction, and fracture. The effects of surgical treatment may be significant if discontinuity of the jaw, or fibrosis of muscles and soft tissue occurs. Radiation fibrosis of muscles and soft tissue and complications of osteoradionecrosis can further affect jaw function [38, 94, 95]. Stress, anxiety and depression associated with cancer heighten psychosocial factors that are often associated with TMD [17, 94–99]. TMD was identified in 1 case, who had combined radiotherapy and surgery that led to extensive muscular fibrosis causing limited mandibular movement and pain. In 2 cases, pain was attributed to TMD due to muscular fibrosis and muscular contraction. In 1 case of persisting pain osteonecrosis was diagnosed with exposure of mandibular bone, 1 case was associated with necrosis of soft tissue of the tongue resulting in a chronic mucosal ulcer. Complaints of persisting mild pain was reported in 4 patients with intact but atrophic mucosa. This was described as sensitivity to spicy, acidic and highly flavoured foods or oral care products. Recurrent tumour was identified in 1 case of persisting pain. The cause of pain was not determined in 25% (3 of 12 cases). Thus, mucosal atrophy was the most common cause of persisting intermittent mild pain in 33% (4 of 12 patients), noted most commonly with eating, or during oral care. TMD was diagnosed in 25% (3 of 12) of patients with persisting pain.

Neuralgia-like pain can develop following surgical treatment. Aching or burning discomfort may be present between episodes of the electric-like pain. Deafferentation (neuropathic) pain may respond to tricyclic medications. These symptoms were identified in 2 patients who had radical neck dissection.

In cases where pain is continuous, systemic analgesics provided on a time contingent basis are required, however, in cases with intermittent or brief pain stimulated by eating, topical agents may be of benefit. During radiotherapy continuous pain was reported in approximately one half of patients due to mucositis.

The length of the questionnaire must be limited. Many of the patients found the questionnaire frustrating to complete, in fact the McGill questionnaire which was included as a part of the survey could not be evaluated due to incomplete forms in the majority of patients. The questionnaire was shortened by elimination of the full McGill questionnaire and may provide a tool for assessment of oral pain due to cancer therapies including radiotherapy and chemotherapy. In addition to determining the frequency and severity of pain in cancer patients, the questionnaire may be used as part of the assessment of interventions planned to manage oral pain.

Summary

The majority of patients with cancer require pain management during the course of their disease. The significance of pain in the head and neck region is magnified because of the importance of the region in development, and psychological and social interactions.

Pain was correlated with the size of the primary tumour. Pain increased during the course of therapy and was experienced by all patients. By the end of radiation therapy, one half of patients had function affected. The medications used did not eliminate pain, and topical and systemic medications were often required in combination. No relation was detected between smoking, the amount smoked and alcohol consumption and pain due to radiation.

In order to better understand pain in the oral cavity and the head and neck in cancer patients more study on incidence, severity, location, aetiology and management is needed. Further research on pain in head and neck cancer will result in several benefits. Prediction of pain during and after treatment will be understood. Patients who are at greater risk of cancer pain may be identified, and therapies directed at pain control can be evaluated. The appropriate time of intervention may be identified. Studies of preventive and therapeutic interventions are needed.

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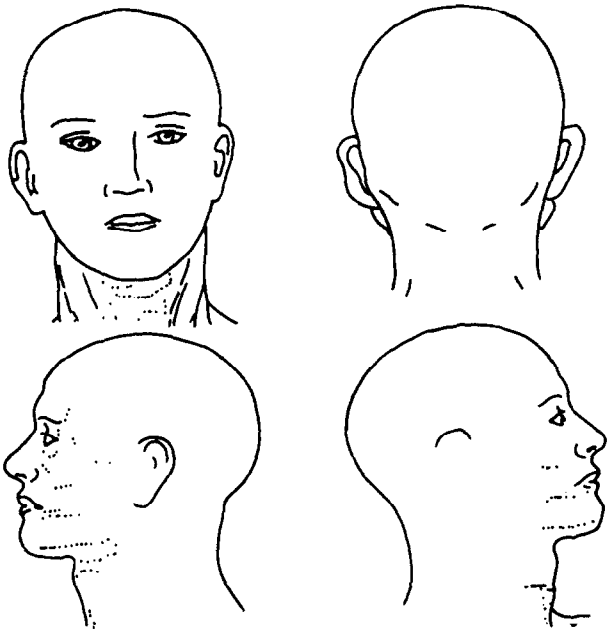
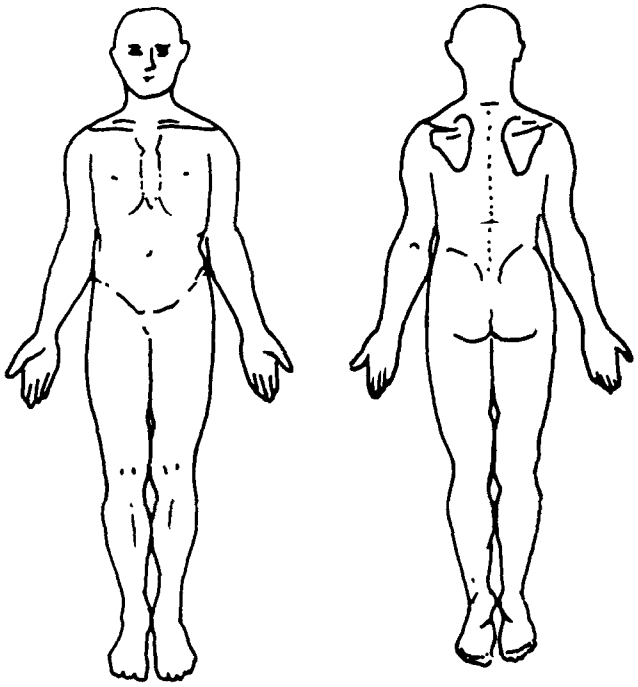
APPENDIX
Head and Neck Pain Profile

1. Name
2. Date
3. Who referred you to the Cancer Control Agency?
   ( ) physician ( ) dentist ( ) other
4. Do you smoke? ( ) no ( ) yes
   If yes, how much?
   ( ) less than 10 cigarettes per day ( ) less than 20 cigarettes per day
   ( ) more than 20 cigarettes per day
5. Do you drink alcohol? ( ) no ( ) yes
   If yes, how much and what type?
6. Do you presently have pain in your mouth, head or neck?
   ( ) no ( ) yes
   If no, please turn to page 5, and answer question 25.
   If yes, please answer the following questions.

7. Shade in the figures below to indicate where the pain in your mouth, head or neck is located.

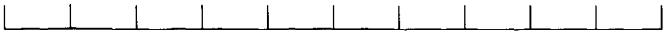


8. Shade in the figures below to indicate any other areas of pain.



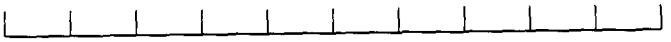
9. Where is your major site of pain? ( ) head or neck ( ) mouth
( ) other
10. How long have you had pain in your mouth, head or neck?
11. Consider the worst pain you have ever felt as 100%. What per cent is your current pain level?
12. Rate the intensity of your pain with a slash (/) along the scales below indicating:
(i) the worst (most severe) pain

No pain — The most intense pain imaginable



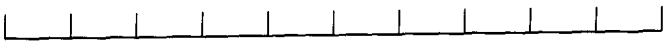
(ii) the usual pain level

No pain — The most intense pain imaginable



(iii) the best (least severe) pain

No pain — The most intense pain imaginable



13. Choose one word that best describes your present pain.
( ) no pain ( ) horrible
( ) mild ( ) excruciating
( ) distressing
14. Are there times during which you experience no pain at all?
( ) no ( ) yes
If yes, how long do these pain free periods last?
15. Is your pain typically worse at any particular time of day?
( ) no ( ) yes
If yes, at what time of day is your pain worse?
( ) morning ( ) evening
( ) afternoon ( ) night
16. What makes your pain worse?
( ) chewing ( ) speaking ( ) other (please specify)
( ) drinking ( ) swallowing
17. How can you lessen your pain?
( ) pain medication (pills) ( ) relaxation techniques
( ) mouth rinses for pain ( ) other (please specify)
( ) soft diet
18. Choose one word group that best describes the pattern of your pain.
( ) continuous, steady, constant
( ) rhythmic, periodic, intermittent
( ) brief, momentary, transient
19. Some of the words below describe your present pain. Circle only one word in each of the 20 groups if the group contains a word that describes your pain. Leave out any group that is not suitable.

Flickering	Jumping	Pricking	Sharp
Quivering	Flashing	Boring	Cutting
Pulsing	Shooting	Drilling	Lacerating
Throbbing		Stabbing	
Beating		Lancinating	
Pounding			
Pinching	Tugging	Hot	Tingling
Pressing	Pulling	Burning	Itchy
Gnawing	Wrenching	Scalding	Smarting
Cramping		Searing	Stinging
Crushing			
Dull	Tender	Tiring	Sickening
Sore	Taut	Exhausting	Suffocating
Hurting	Rasping		
Aching	Splitting		
Heavy			
Fearful	Punishing	Wretched	Annoying
Frightful	Gruelling	Blinding	Troublesome
Terrifying	Cruel		Miserable
	Vicious		Intense
	Killing		Unbearable
Spreading	Tight	Cool	Nagging
Radiating	Numb	Cold	Nauscating
Penetrating	Drawing	Freezing	Agonizing
Piercing	Squeezing		Dreadful
	Tearing		

20. List the types of treatment you have tried for your pain problem.

		Effective	
1.	_____	( ) no	( ) yes
2.	_____	( ) no	( ) yes
3.	_____	( ) no	( ) yes
4.	_____	( ) no	( ) yes

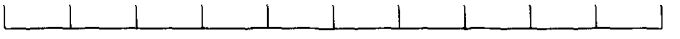
21. List any types of treatment you are interested in trying.
    1. _____
    2. _____
    3. _____
    4. _____

22. List the medications you are currently taking for your pain and the average number taken per day (or per week).

	Medication name and dosage	Amount or number taken daily
1.	_____	_____
2.	_____	_____
3.	_____	_____
4.	_____	_____

23. Rate how much pain has interfered with your functioning within the past week by placing a slash (/) along the scale below.

The pain has not interfered at all — I have been totally disabled



24. How likely do you feel that your pain will be removed or cured?
    ( ) impossible ( ) likely
    ( ) unlikely ( ) certain
    ( ) uncertain
25. How do you think the doctors can help to alleviate your pain?
26. How do you think the dentist can help to alleviate your pain?
27. Please feel free to make any additional comments.