RESEARCH ARTICLE

Uncertainties in the choice of dose and elective volumes during postoperative radiotherapy for cutaneous squamous cell carcinoma with perineural invasion.

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Abstract:

Introduction: Post-operative radiotherapy (PORT) for resected cutaneous squamous cell carcinoma (CSCC) with perineural invasion (PNI) is controversial. Therefore, we conducted a survey to study the patterns of practice and determine whether there is a consensus among Radiation Oncologists (ROs) regarding prescribed dose to the post-operative bed and elective treatment of lymph nodal regions and neural pathways. We also compared the recommendations of the ROs with the 2010 NCCN guidelines.

Materials & Methods: In March 2011, we contacted all ROs and trainees residing in the USA through their email address listed in the 2009 ASTRO membership directory. Our survey contained clinical vignettes involving Mohs micrographically resected CSCC with microscopic PNI (mPNI) or clinical (symptomatic or radiographic) cPNI, including named nerve PNI (nPNI). For each vignette, physicians indicated if PORT was appropriate and further specified the dose and volume to treat at standard fractionation. Chemotherapy was not allowed. Responses were stratified according to years of post-residency experience, special interest in treating head and neck cancers and number of cases treated per year. We defined consensus as 80% concordance.

Results: Three hundred and fifty two responses were completed and analyzed. Approximately 95% recommended PORT for cPNI whereas a mean of 59% recommended PORT for mPNI. There was no consensus regarding dose to the operative bed. Approximately 30% of respondents prescribed 54 Gy or less at standard fractionation, while the NCCN guidelines recommend 60 Gy in 30 fractions. Only 24% were willing to prescribe 66Gy or more in cases of radiographically identified gross residual disease. In cases of mPNI, there was a consensus not to treat elective nodal volumes; on average only 14% treated elective nodal regions. Even in the presence of cPNI, only 40% recommended elective nodal irradiation (ENI). ROs with over ten years' experience were more willing to offer ENI for cPNI than less experienced ROs (43% vs. 25% p=0.004). For mPNI, there was no consensus for elective neural pathway irradiation (ENP); whereas for cPNI a clear consensus emerged with over 90% recommending ENP. The NCCN guidelines do not have specific recommendations for ENI or ENP. Stratification based on years of post-residency experience (<10 vs. 10+ yrs), number of cases treated per year (0-7 vs. 8+ cases per year) and special interest in treating head and neck cancers did not yield any other statistically significant differences.

Conclusions: Our data from 2011 demonstrates a lack of consensus among ROs regarding radiation dose to the post-operative bed and designation of elective targets (i.e. nodal regions and neural pathways) for resected CSCC with PNI. In contrast to the NCCN guidelines, nearly 30% of ROs under-dosed the post-operative bed. Majority of ROs omitted elective nodal irradiation even in cases of cPNI. While there was a consensus to treat ENP for cPNI, there was wide variability for treating ENP for mPNI. Since this survey was conducted, several guidelines have been published to educate radiation oncologists regarding electively targeting the neural pathways. Updated data to evaluate the impact of these guidelines is needed in this setting to guide ROs and achieve homogenous practice patterns.

Keywords: perineural invasion, radiotherapy, cutaneous squamous cancers

Introduction:

An estimated 700,000 new cases of CSCC are diagnosed each year in the US, resulting in approximately 2,500 deaths and the incidence continues to rise [1-3]. Perineural invasion (PNI) is found in 2-15% of CSCC patients. It is an independent poor prognostic factor with metastatic rates as high as 47% and 3-year disease specific mortality rate of 30% [4-7].

Perineural invasion (PNI) is defined as the presence of malignant cells within the perineural space of nerves [8]. PNI may be classified into two broad categories - microscopic PNI (mPNI) or more extensive clinical PNI (cPNI) [9]. mPNI is defined as involvement of small, peripheral, unnamed nerves usually of the reticular dermis and less often subcutaneously found incidentally in an asymptomatic patient's pathology specimen. It cannot be detected on radiographic studies and by definition is not associated with signs or symptoms. Patients with cPNI may have neurologic symptoms (such as pain, parasthesia, or weakness), radiographic evidence of disease, and/or named (large) nerve involvement (nPNI) that is macroscopically detected during surgery.

It is estimated that 60-70% of all cases of PNI in CSCC have mPNI [9]. The prognosis of cPNI is significantly worse than mPNI with local control rates of approximately 50% vs. 80-90% respectively. Local control with cPNI that extends to the skull base is only 25% and long-term survival with cPNI is approximately 20–30% [6, 9-13]. Most of the studies of CSCC with PNI have reported using post-operative radiotherapy (PORT) [9, 14]. However, the details of radiation dose and the volume irradiated during PORT varied across studies and have not been consistently reported [5-7,9-15].

In a prospective randomized trial the optimal dose in conventionally fractionated PORT for head and neck cancer was established by Peters et al [16]. In this study, patients were randomized to one of three dose levels ranging between 52.2 Gy and 68.4 Gy, all given in daily doses of 1.8 Gy. Those who received a dose of 54 Gy or less had a significantly higher failure rate than those receiving 57.6 Gy.

Goepfert et al reported a 35% incidence of lymph nodal metastases in cases of CSCC with PNI making a case for elective nodal irradiation (ENI) [6]. In a study by Garcia-Serra et al, 18% of mPNI and 44% of cPNI cases received ENI [12]. Regional nodal recurrence as the initial site of relapse in this study was 14% for mPNI and 5% for cPNI, respectively. These results highlight the importance of ENI in patients with CSCC with PNI in whom the lymph nodes are clinically uninvolved.

Skip metastases and tumor extensions along nerve pathways for distances upto 14 cm have been reported in CSCC with PNI, which argues for elective neural pathway irradiation (ENP) [6-8,17]. Both, centripetal and centrifugal spreads have been documented [18]. Gluck et al emphasized on ENP in their recent report of post radiotherapy failure patterns in head and neck CSCC with PNI [19]. The most prevalent failure pattern in their study was along cranial nerves (in particular V and VII), and multiple cranial nerves were ultimately involved in the majority of cases. In all cases the involved cranial nerves at recurrence were the main nerves innervating the primary tumor sites, as well as their major communicating nerves.

However, a concern for toxicity of treatment may preclude ROs from electively treating nodal regions (ENI) and/or nerve pathways (ENP) that may be at risk for occult disease spread. Garcia-Serra et al reported that 10% of patients treated with PORT for mPNI and 33% treated for cPNI had treatment-related toxicity, including soft

tissue necrosis, bone exposure, and osteoradionecrosis [12].

Some of the uncertainties and controversies in the literature are reflected in a survey of Mohs surgeons that demonstrated a great variability in the management of CSCC with PNI including indications for radiotherapy referral [20]. The practice patterns among Radiation Oncologists (ROs) in the management of CSCC with PNI are unknown. Therefore, we designed a web based survey for ROs to determine whether there is a consensus among ROs regarding:

1. Radiotherapy dose to the post-operative bed
2. Elective treatment of lymph nodal regions (ENI)
3. Elective treatment of neural pathways (ENP)

We also compared their recommendations with the 2010 NCCN guidelines.

In a separate publication (Parvathaneni et al.), we have reported the results of RO recommendations for utilizing PORT in standardized cases of CSCC with PNI.

Materials & Methods:

This study was approved by the Institutional Review Board (IRB) of the University of Washington and Fred Hutchinson Cancer Consortium.

Participants

In March 2011, we conducted a web based survey of all ROs and trainees residing in the USA with an email address listed in the 2009 ASTRO directory. We invited all physicians via email and then contacted non-responders every two weeks for a total of three cycles. Collected data was de-identified and stored using www.surveymonkey.com to protect responders' privacy.

Respondents also provided demographic information i.e. years of post-residency experience, special interest in treating head and neck cancers, number of cases of CSCC with PNI treated per year and whether they practiced in an academic vs. private setting.

Survey Design

We defined a standardized patient as a healthy 50 year old asymptomatic male who is status post Mohs surgical resection of a 1.0 cm well differentiated CSSC of the infra orbital medial cheek region that is confined to the dermis. Negative margins were obtained after two stages of excisions. There were no clinical symptoms suggestive of cPNI (i.e. numbness, parasthesias, weakness), nor radiographic evidence of PNI on an MRI. There was no clinical or radiographic evidence of lymph node involvement. Adjuvant chemotherapy was not an available option.

In the first clinical vignette, the standardized patient presents with an incidentally detected mPNI and ROs were asked if they would recommend PORT (Figure 1). If they did recommend PORT, the RO then specified the dose used at standard fractionation (i.e 1.8-2Gy per fraction) as well as volume they would treat i.e to the operative bed and/or any elective treatment to lymph nodal regions or neural pathways (Figure 2).

Figure 1: Sample Clinical Vignette

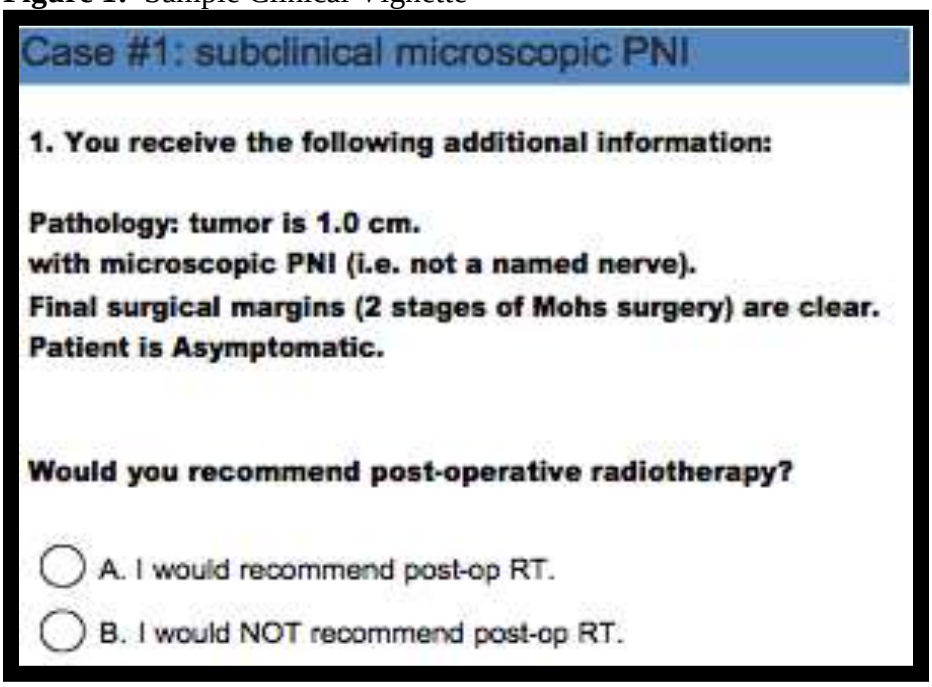
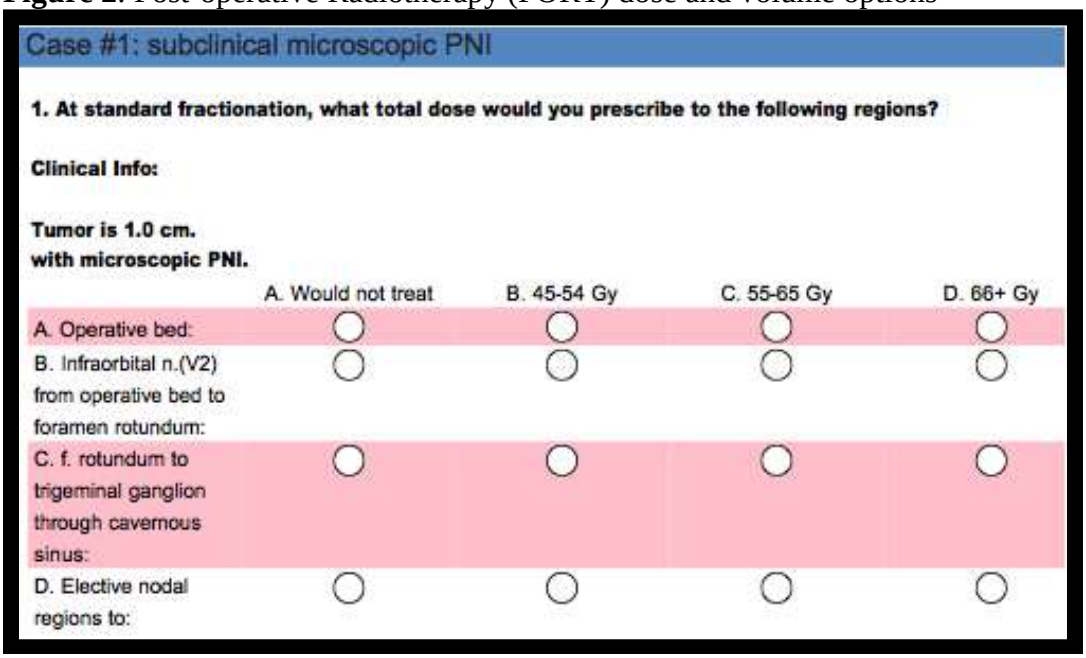


Figure 2: Post-operative Radiotherapy (PORT) dose and volume options



Six subsequent vignettes followed (table 1). Each introduced one additional poor prognostic factor i.e. immunosuppression (renal transplant patient), deep subcutaneous non-named nerve invasion (sPNI) requiring a third stage for clearance, more extensive clinical PNI (cPNI) involving a symptomatic patient with and without radiographically detectable PNI and PNI involving a named nerve (nPNI). In each case, physicians indicated if PORT was appropriate followed by the recommendations for dose and treatment volume at standard fractionation.

Table 1: Clinical vignettes

The standardized patient : 50 year old asymptomatic male who is status post Mohs surgical resection of a 1.0 cm well differentiated CSSC of the infra orbital medial cheek region that is confined to the dermis. Negative margins were obtained after two stages of excisions. You receive the following additional information:
1. Pathology: tumor is 1.0 cm with mPNI.
2. Patient had a renal transplant and is on **immunosuppressive medications**. Pathology: tumor is 1.0 cm. with mPNI.
3. Pathology: tumor is 1.0 cm with mPNI. Tumor **extends deep** along a **non-named subcutaneous nerve and required a third Mohs stage** for clearance. Post-op MRI shows no evidence of disease.
4. Pathology: tumor is 1.0 cm. with mPNI. **Pre-op exam revealed numbness along V2 distribution**. Post-op MRI shows no evidence of disease.
5. Pathology: tumor is 1.0 cm. with **PNI involving the infraorbital nerve**. Tumor required excision through the infraorbital foramen. Patient is asymptomatic. Post-op MRI shows no evidence of disease.
6. As in 5, AND **Pre-op exam showed numbness along V2 distribution**. Post-op MRI shows no evidence of disease.
7. As in 6, AND **Post-op MRI shows evidence of thickening/enhancement of infraorbital nerve (V2) proximally up to the foramen rotundum**.

Abbreviations: mPNI is microscopic PNI of incidental non, named nerve detected on patient's pathology specimen. nPNI is PNI of a named nerve, in this case the infraorbital nerve. cPNI is PNI which is either symptomatic (eg: numbness in V2 distribution) or has radiologically detectable tumor. NB: nPNI is also considered as cPNI.

Statistical Analysis

We defined consensus as 80% concordance/agreement among responses. All statistical analyses were performed using SPSS version 16. We used standard descriptive statistics and frequency tabulation. Associations between percentage of ROs and their recommendations for Dose (45-54 Gy, 55-65Gy and >66Gy), ENI and ENP for each vignette were assessed by cross-tabulation and 95% confidence intervals calculated using the Wald method. Treatment recommendations for ENI and ENP were considered without any absolute minimum threshold dose. Any prescribed dose (ranging from 45 to 66+Gy) was considered as a treatment recommendation since these were elective targets. Responses were stratified according to years of post-residency experience (<10 yrs vs. 10+ yrs),

special interest in treating head and neck cancers and number of cases treated per year (0-7 cases vs. 8+ cases). Associations between sub-categorical variables were assessed via cross-tabulation and Fisher's exact test to generate two tailed p values and differences were considered statistically significant when the p value was < 0.05.

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Table 2: Characteristics of Survey Respondents

Variable	Total % of respondents (n=352)
Years Post-Residency	
1-3	8 (29)
3-5	5 (16)
5-10	11 (40)
10+	70 (245)
Currently in residency	6 (21)
Practice Location	
Academic	32(102)
Private	57(183)
Both	11 (34)
Special Interest in treating H & N cancer?	
Yes	64(207)
No	36(115)
Number of CSCC with PNI cases treated in past year	
0-3	36(117)
4-7	38(123)
8-10	16(51)
11 or more	10(34)

Results:

Demographics:

Three thousand six hundred eighty eight physicians were contacted to participate in our survey. Three hundred sixty eight of the email addresses were undeliverable for various reasons. Six hundred thirty six opened the survey. One

hundred ten responded requesting not to participate in this or any other surveys in the future due to a lack of time. One hundred eighty four responded indicating they preferred not to participate in this survey due to a lack of experience in treating CSCC with PNI. Finally, 352 completed responses were eligible for analysis. Characteristics of the responders are listed in Table 2. Respondents were closely split between private and academic practitioners. If they were diagnosed with CSCC with PNI, 62% would prefer their care by an RO specializing in head & neck cancer at an academic center (due to a higher case volume compared to a Generalist). Approximately 95% recommended PORT for cPNI whereas a mean of 59% recommended PORT for mPNI

Dose to the Post-operative bed

There was no consensus regarding dose to the operative bed (Table 3). Approximately 30% of respondents prescribed 54 Gy or less at standard fractionation, while the NCCN guidelines recommend 60 Gy in 30 fractions. Only 24% (95% CI: 13.85-34.15) were willing to deliver 66Gy or more in cases of radiographically identified gross residual disease while the guidelines recommend treating gross disease to 66-70 Gy. For gross residual disease, 64% (95% CI: 56.95-71.05) prescribed between 55-65Gy.

Table 3: Dose to Post-operative bed

Clinical Scenario	% prescribing 45-54 Gy	95% CI
mPNI in asymptomatic patient	33	24.98 - 41.02
mPNI in asympt. immune suppressed patient	33	26.26 - 39.74
deep subcutaneous non-named nerve invasion	32	25.86 - 38.14
V2 numbness but non-named nerve, MRI negative	29	23.35 - 34.65
nPNI in asympt. patient, MRI negative	26	20.83 - 31.17
nPNI with V2 numbness MRI negative	25	19.9 - 30.1
cPNI with tumor detected on MRI and V2 numbness	12	8.19 - 15.81

Elective Nodal Irradiation (ENI)

For cases of mPNI, there was a consensus not to treat elective nodal regions (table 4); on average, 86% would not treat ENI. In the presence of cPNI, although there was a lack of consensus, a majority would not treat ENI. A maximum of 39% recommended ENI even in an extreme case of cPNI with gross residual disease. ROs with over ten years' experience were more willing to offer ENI for cPNI than less experienced ROs (43% vs. 25% p=0.004). Almost all the ROs treating ENI used a dose of 45-54Gy, which is appropriate. The NCCN guidelines state that PNI poses an increased risk for metastases and ENI (50 Gy at 2 Gy per fraction) is suggested for "lymph nodes that are at risk for sub clinical disease". But they do not make any direct recommendations for ENI for CSCC with PNI.

Table 4: ENI recommendations

Clinical Scenario	% recommending ENI	95% CI
mPNI in asymptomatic patient	13	0.08 - 0.20
mPNI in asympt. immune suppressed patient	11	0.16 - 0.28
deep subcutaneous non-named nerve invasion	18	0.14 - 0.25
cPNI - V2 numbness but non-named nerve, MRI negative	24	0.19 - 0.29
nPNI in asympt. patient, MRI negative	30	0.25 - 0.36
nPNI with V2 numbness MRI negative	32	0.27 - 0.38
cPNI with tumor detected on MRI and V2 numbness	39	0.33 - 0.44

Elective Nerve Pathway Irradiation (ENP)

Overall, there was no consensus for any elective neural pathway irradiation (ENP) for cases of mPNI; whereas for cPNI a clear consensus emerged with over 90% recommending ENP (table 5). Over 40% of ROs recommended an ENP dose greater than 55 Gy for cPNI whereas fewer than 20% recommended a dose greater than 54 Gy for mPNI. The NCCN guidelines do not have any recommendations for ENP. We sub categorized ENP to examine RO recommendations for irradiating the nerve pathways through the cavernous sinus and trigeminal ganglion at the skull base i.e proximal ENP (proximal to the foramen rotundum). We found that for mPNI, there was a consensus with nearly 80% not recommending proximal ENP (table 6). For cPNI, with each additional poor prognostic factor such as named nerve involvement - nPNI, symptomatic nPNI and finally cPNI with gross residual disease, there was a greater willingness to offer treatment.

Table 5: ENP recommendations

Clinical Scenario	% recommending ENP	95% CI
mPNI in asymptomatic patient	38	0.30 - 0.46
mPNI in asympt. immune suppressed patient	52	0.45 - 0.59
deep subcutaneous non-named nerve invasion	64	0.50 - 0.70
cPNI - V2 numbness but non-named nerve, MRI negative	97	0.94 - 0.99
nPNI in asympt. patient, MRI negative	99	0.98 - 0.99
nPNI with V2 numbness MRI negative	100	0.98 - 0.99
cPNI with tumor detected on MRI and V2 numbness	100	0.98 - 0.99

Table 6: proximal ENP irradiation to the skull base

Clinical Scenario	% recommending proximal ENP to skull base	95% CI
mPNI in asymptomatic patient	11	0.06 - 0.17
mPNI in asympt. immune suppressed patient	18	0.13 - 0.24
deep subcutaneous non-named nerve invasion	22	0.17 - 0.28
cPNI - V2 numbness but unnamed nerve, MRI negative	51	0.45 - 0.57
nPNI in asympt. patient, MRI negative	76	0.71 - 0.81
nPNI with V2 numbness MRI negative	82	0.77 - 0.86
cPNI with tumor detected on MRI and V2 numbness	97	0.95 - 0.99

Sub group analyses

Stratification based on years of post-residency experience (<10 vs. 10+ yrs), number of cases treated per year (0-7 vs. 8+ cases per year) and special interest in treating head and neck cancers did not yield any other statistically significant differences apart from the one mentioned above for ENI.

Discussion:

CSCC is a common cancer and 2-15% of cases are diagnosed with PNI, which is an independent poor prognostic factor. PNI appears to have a spectrum of prognosis with local control rates of 80-90% reported for mPNI and 25-50% for cPNI [9], and there is wide variation among practitioners managing this entity [20]. To our knowledge, this is the first study that examines the patterns of practice among ROs in the management of CSCC with PNI. In a separate publication [21], we reported that our study demonstrates a wide variability among ROs in the management of CSCC with mPNI without any consensus for recommending PORT. For cases of cPNI, an overwhelming majority recommended PORT. In this article, we focus on the dose and volume considerations and compare RO recommendations with the NCCN 2010 guidelines. Our data suggests a lack of consensus among ROs regarding radiation dose to the post-operative bed and designation of elective targets (i.e. nodal regions and neural pathways). In contrast to the NCCN guidelines, nearly 30% of ROs under-dosed the post-operative bed to 54Gy or less, and 76% prescribed less than 66Gy for gross residual disease. Over 60% of ROs omitted ENI even in cases of cPNI. While there was a consensus to treat ENP for cPNI, there was wide variability for mPNI.

The dose to the post-operative bed has been well established by Peters et al, although their study was based on head and neck mucosal primaries [16]. To our knowledge, there are no other high quality dose response studies for CSCC. The NCCN guidelines recommend 60 Gy in 30 fractions and it is unclear why 30% of ROs would recommend 54Gy or less in standard fractionation to the operative bed. Seventy six percent of the ROs prescribed a dose less than 66Gy to the gross residual disease near the skull base. This may be explained by the

presence of dose limiting critical structures (optic structures, cochlea, brain stem) in the vicinity. In this survey, we did not allow ROs to specify the technical particulars of boosting gross disease at the skull base; we explored only the total dose in standard fractionation that would be prescribed to treat gross residual disease. We speculate that several providers might have chosen to boost with gamma knife, or cyber knife, if available and these modalities might utilize a fraction size greater than the standard 1.8-2Gy. Nevertheless, a total dose of less than 66Gy for gross residual disease is unlikely to be curative.

Elective nodal irradiation (ENI) appears to be utilized by a minority of ROs. On average, 86% of ROs did not recommend ENI for mPNI and only 31% recommended for cPNI. Jackson et al reported that 55% of failures among the CSCC with mPNI in their study were nodal failures [15]. Only 1% of the patients in their study received ENI. In a study by Garcia-Serra et al, almost half of the recurrences in patients with mPNI were limited to the first-echelon regional nodes [12]. 18% of mPNI and 44% of cPNI cases received ENI . Regional nodal recurrence as the initial site of relapse in this study was 14% for mPNI and 5% for cPNI, respectively. They recommend ENI for all cases of CSCC with PNI. The NCCN guidelines do not make any direct recommendations for ENI for CSCC with PNI, but they state that PNI poses an increased risk for metastases and ENI is suggested for "lymph nodes that are at risk for sub clinical disease".

The limited utilization of ENI appears to stem from concerns of toxicity. Garcia-Serra et al reported that 10% of patients treated with PORT for mPNI and 33% treated for cPNI had treatment-related toxicity, including soft tissue necrosis, bone exposure, and osteoradionecrosis [12]. However, these data were generated from patients treated between 1965 to1999, predominantly with historical radiotherapy techniques. Modern treatment with Intensity Modulated Radiation therapy (IMRT) is safer and significantly less morbid. A prospective randomized clinical trial demonstrated that IMRT is significantly superior to historical technique in sparing salivary glands [22]. The consequential recovery of salivary function, reduced the incidence of xerostomia with marked improvements in associated quality of life. IMRT can also spare other normal structures such as cochlea, oral mucosa, temporo mandibular joint, and mandible [23,24]. Complications such as osteonecrosis are rare in patients treated with IMRT and adequate supportive dental care. Ben David et al reported on 176 patients with head and neck cancer treated with parotid gland-sparing IMRT between 1996 to 2005 [24]. These patients also underwent a dental prophylaxis and extractions of high-risk, periodontally involved, and non-restorable teeth. The IMRT plans included dose constraints for the maximal mandibular doses, mean parotid gland and uninvolved oral cavity doses. None of the patients developed osteoradionecrosis at a median follow-up of 34 months in this study. Proton therapy might reduce this toxicity profile even further [25].

Elective neural pathway irradiation (ENP) appears to be more popular than ENI for CSCC with PNI. Over 90% recommended ENP for cPNI and on average 51% recommended it for mPNI. This has been validated in a recent study of head and neck CSCC with PNI. Gluck et al reported that the most prevalent failure pattern was along cranial nerves innervating the primary tumor sites (in particular V and VII), as well as their major communicating nerves [19]. In this survey, we used a case with a primary CSCC arising in the medial cheek below the eye, (infra orbital nerve distribution) and

tried to evaluate RO recommendations for irradiating the proximal trigeminal nerve pathway through the cavernous sinus and trigeminal ganglion (proximal ENP). We found that on average 76.5% of ROs recommended proximal ENP for cPNI and only 17% for mPNI. The NCCN 2010 guidelines do not make any recommendations for ENP. However, there are now several published guidelines that aim to educate radiation oncologists regarding targeting elective neural pathways [26-29]. In addition, the NCCN 2019 guidelines recommend including the course of the local nerves proximally in cases of extensive perineural invasion, clinically evident perineural involvement, or involvement of named nerves in the head and neck region.

Our study is subject to certain limitations. Some caution is required in interpreting the results of any voluntary survey. Selection bias and sampling errors are inherent issues as respondents usually represent a "self-selected" group with an interest in the topic and their views may not reflect those of the wider community of clinicians thus, limiting their generalizability. For example, the majority (70%) of ROs that responded to our survey had greater than 10 years of experience, and 64% had a self-identified special interest in treating Head and neck cancers. However, sub group stratification analysis based on years of post-residency experience (<10 vs. 10+ yrs), number of cases treated per year case (0-7 vs. 8+ cases per year) and special interest in treating head and neck cancers did not yield any statistically significant differences apart from the one mentioned above for ENI. The overall response rate to this survey was approximately 10%. However, the completion rate, which represents the ratio of opened and completed surveys was 55% which is within the reference range for an e-mail–based survey [30]. Moreover, there were 352 completed responses that could be analyzed and this number is consistent with other recent large-scale radiation oncology survey studies [30-36]. Our survey was open to all ROs, regardless of interest or experience with a relatively uncommon clinical scenario. In fact, 184 ROs responded that they lack the expertise /experience with CSCC with PNI to participate in this survey. Surveys that target practitioners with a special interest in a particular topic tend to receive a higher response rate [20,37]. While the response percent appears better in these studies, it does not increase their statistical power which is based on the absolute number of analyzable responses. The number of completed responses in our survey (n=352) compare well with the survey of Mohs surgeons (n=118), although their response rate is higher at 47% due the fewer invited participants [20]. Hence, we believe the findings and the statistical significance of the results of our survey at the time it was conducted are valid.

Conclusion:

There was a general lack of consensus among U.S based ROs regarding radiation dose to the post-operative bed and designation of elective targets (i.e. nodal regions and neural pathways) for resected CSCC with PNI. Thirty percent of ROs under-dosed the post-operative bed. Seventy six percent prescribed less than 66Gy for gross residual disease, probably due to the dose limiting critical structures located in the vicinity of the skull base. Majority of ROs omitted elective nodal irradiation even in cases of cPNI. While there was a consensus to treat ENP for cPNI, there was wide variability for mPNI. With the publication of several guidelines since this survey was conducted, more data is needed in this setting to assess their impact on ROs in an attempt to achieve homogenous practice patterns.

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