

# Comparison of Electronic Brachytherapy and Mohs Micrographic Surgery for the Treatment of Early-Stage Non-Melanoma Skin Cancer: A Matched Pair Cohort Study

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## PURPOSE

High dose rate electronic brachytherapy (EBX) provides a non-surgical treatment option for non-melanoma skin cancer (NMSC). This matched-pair cohort study compared the outcomes of treatment with EBX to those of Mohs micrographic surgery (MMS) in patients with NMSC.

## METHODS

All patients who had already received EBX for NMSC at 4 clinical sites and met the eligibility criteria were invited to participate. EBX was previously administered using the Xofo® Axcent® Electronic Brachytherapy System® (Xofo, Inc., A Subsidiary of iCAD, Inc. San Jose, CA). Standard surface applicators (Xofo, Inc.) included sizes 10, 20, 35, and 50 mm in diameter and EBX was administered in 8-10 fractions twice per week, with a dose per fraction of 4, 4.5 or 5 Gy, to an average depth of 3mm. MMS was previously performed by clinicians who had completed Mohs fellowship training, and surgeries were conducted according to guidelines of the ACMS. The EBX participants were individually matched with MMS patients based on patient age, lesion size ( $\leq 1$ cm,  $>1$ cm  $\leq 2$ cm,  $>2$ cm  $\leq 3$ cm) type, and location (head, nose, torso, upper extremity, lower extremity), and treatment dates. Eligibility criteria included: Completion of EBX or MMS for NMSC  $\geq 3$  years prior to enrollment; age  $>40$  years; pathological diagnosis confirmed (SCC, BCC) prior to treatment; cancer stage 0-2. Exclusion criteria included: Target area adjacent to a burn scar; surgical resection of the cancer prior to EBX; known metastatic disease. Data were collected prospectively at an office visit, during which patients were clinically evaluated by the physician who had conducted the EBX or MMS, and each participant completed a questionnaire.

## RESULTS

The 369 patients (188 in the EBX treatment group and 181 in the MMS treatment group) had 416 lesions (208 in the EBX group and 208 in the MMS group), including 226 basal cell carcinomas (BCC) and 190 squamous cell carcinomas (SCC). Most patients were Caucasian (98.9% and 99.5%) and male (65.4% and 66.3%) of median age 80.7 (EBX) and 76.8 years (MMS). Most lesions were size  $>1$  cm and  $\leq 2$  cm, and located on the head (Ear/Eyelid/Face/Neck/Lip/Scalp), 59.2% in each group. At follow up, 66.7% of EBX and 68.8% showed a relatively invisible scar ( $p=ns$ ). 99.5% of EBX and 100.0% of MMS-treated lesions were recurrence-free ( $p=ns$ ). Physicians rated cosmesis as "Excellent" or "Good" in 97.6% and 95.7% of EBX-treated and MMS-treated lesions respectively ( $p=ns$ ).

## CONCLUSION

Recurrence rates and patient reported outcomes with EBX and MMS were similar at a mean of 3.4 years following treatment of NMSC.



Table 1. Patient Demographics at Time of Treatment

Variable		EBX	MMS	
Number of Patients (%)		188	181	
Age (years)	Median	80.7	76.8	
	Range	61.1 – 98.0	51.4 – 98.4	
Gender	Male	123 (65.4%)	120 (66.3%)	
	Female	65 (34.6%)	61 (33.7%)	
Ethnicity	Caucasian/Non-Hispanic	186 (98.9%)	180 (99.5%)	
	African-American	0 (0.0%)	1 (0.5%)	
	Asian/Pacific Islander	2 (1.1%)	0 (0.0%)	
Prior skin cancer	Prior skin cancer	147 (78.2%)	136 (75.1%)	
	Types:	Melanoma	13 (6.9%)	8 (4.4%)
		BCC	135 (71.8%)	114 (63.0%)
		SCC	105 (55.9%)	97 (53.6%)
BSC	1 (0.5%)	0 (0.0%)		
Prior surgery or treatment of another lesion		57 (30.3%)	124 (68.5%)	

EBX=electronic brachytherapy; MMS=Mohs micrographic surgery;  
BCC=basal cell carcinoma;  
SCC=squamous cell carcinoma; BSC=basosquamous carcinoma

Table 2. Lesion Characteristics at Time of Treatment

Variable		EBX	MMS
Number of Lesions (%)		208	208
Histopathology	BCC	113 (54.3%)	113 (54.3%)
	SCC	95 (45.7%)	95 (45.7%)
Cancer Staging <sup>1</sup>	Stage 0: Tis, NO, MO	101 (48.6%)	76 (36.5%)
	Stage 1: T1, NO, MO	103 (49.5%)	129 (62.0%)
	Stage 2: T2, NO, MO & $\leq 4$ cm in diameter	4 (1.9%)	3 (1.4%)
Lesion Size (cm)	$\leq 1$ cm	57 (27.4%)	57 (27.4%)
	$> 1$ cm and $\leq 2$ cm	146 (70.2%)	146 (70.2%)
	$> 2$ cm and $\leq 3$ cm	5 (2.4%)	5 (2.4%)
Lesion Location	Head	5 (2.4%)	5 (2.4%)
	Ear	10 (4.8%)	10 (4.8%)
	Eyelid	5 (2.4%)	5 (2.4%)
	Face/Neck	72 (34.6%)	72 (34.6%)
	Lip	4 (1.9%)	4 (1.9%)
	Scalp	14 (6.7%)	14 (6.7%)
	Nose	33 (15.9%)	33 (15.9%)
	Torso	12 (5.8%)	12 (5.8%)
	Lower Extremity	23 (11.1%)	23 (11.1%)
	Upper Extremity	30 (14.4%)	30 (14.4%)

EBX=electronic brachytherapy; MMS=Mohs micrographic surgery; BCC=basal cell carcinoma; SCC=squamous cell carcinoma; T=tumor; N=nodes (lymph); M=metastases; G=grade  
1. Cancer Staging System of the American Joint Committee on Cancer

Table 3. Treatment Characteristics for Electronic Brachytherapy (EBX)

Variable		208
Number of Lesions (%)		208
Applicator Size (mm)	10 mm	78 (37.5%)
	20 mm	103 (49.5%)
	35 mm	25 (12.0%)
	50 mm	2 (1.0%)
Total Received Dose	32 Gy	5 (2.4%)
	36 Gy	1 (0.5%)
	40 Gy	207 (99.5%)
	50 Gy	1 (0.5%)
Number of Fractions	8/8	198 (95.2%)
	10/10	10 (4.8%)
Dose per Fraction	4 Gy	14 (6.7%)
	4.5 Gy	1 (0.5%)
	5 Gy	193 (92.8%)

Table 4. Treatment Characteristics for Mohs Micrographic Surgery (MMS)

Variable		n= 208
Number of Lesions (%)		208
Stages/levels required for clear margins	1	177 (85.1%)
	2	30 (14.4%)
	3	1 (0.5%)
Closure method	Surgical Closure	192 (92.3%)
	Secondary Intention	16 (7.7%)

Table 8. Results of Patient Satisfaction Questionnaire at Followup Visit

	EBX n=208	MMS n=208
Total Score		
Mean $\pm$ Std	54.0 $\pm$ 9.0	56.0 $\pm$ 5.3
Median [Range]	58.0 [10 – 60]	59.0 [38 – 60]
Individual Questions <sup>2</sup>		
Treatments were convenient (5=strongly agree)	4.3 $\pm$ 1.1 5.0 [0 – 5]	4.7 $\pm$ 0.6 5.0 [2 – 5]
Satisfied with how well treatment worked (5=strongly agree)	4.5 $\pm$ 1.0 5.0 [0 – 5]	4.8 $\pm$ 0.5 5.0 [1 – 5]
Satisfied with appearance of the treated area (5=strongly agree)	4.4 $\pm$ 1.0 5.0 [0 – 5]	4.6 $\pm$ 0.7 5.0 [2 – 5]
If another cancer, would use same treatment (5=strongly agree)	4.1 $\pm$ 1.4 5.0 [0 – 5]	4.6 $\pm$ 0.7 5.0 [1 – 5]
Have not had any skin problems with treated area (5=strongly agree)	4.5 $\pm$ 1.2 5.0 [0 – 5]	4.7 $\pm$ 0.6 5.0 [1 – 5]
Since treatment, frustrated about appearance of treated site (5=strongly disagree)	4.5 $\pm$ 1.1 5.0 [0 – 5]	4.6 $\pm$ 1.0 5.0 [0 – 5]
Since treatment, embarrassed about appearance of treated site (5=strongly disagree)	4.6 $\pm$ 0.9 5.0 [0 – 5]	4.7 $\pm$ 0.7 5.0 [1 – 5]
Since treatment, depressed about appearance of treated site (5=strongly disagree)	4.5 $\pm$ 1.1 5.0 [0 – 5]	4.6 $\pm$ 0.8 5.0 [0 – 5]
Treatment prevented me from participating in daily activities (5=strongly disagree)	4.6 $\pm$ 0.9 5.0 [0 – 5]	4.6 $\pm$ 0.9 5.0 [0 – 5]
Treatment made it hard to work or do what I enjoy (5=strongly disagree)	4.7 $\pm$ 0.7 5.0 [0 – 5]	4.6 $\pm$ 0.8 5.0 [0 – 5]
Would recommend treatment to others (5=strongly agree)	4.4 $\pm$ 1.3 5.0 [0 – 5]	4.7 $\pm$ 0.7 5.0 [0 – 5]
Always followed instructions related to care of treated area (5=strongly agree)	4.9 $\pm$ 0.4 5.0 [3 – 5]	4.7 $\pm$ 0.5 5.0 [2 – 5]

Std=standard deviation

2. A score of 5 represents the maximum positive or favorable response to each question.

Table 5. Primary Endpoint: Absence of Local Recurrence at Followup Visit

Variable	EBX	MMS	
Number of Lesions (%)	208	208	
Absence of Local Recurrence	207 (99.5%)	208 (100.0%)	
95% CI:	97.4% - 100%	98.2% - 100%	
p-value (Fisher's Exact Test):	1.000		
Follow-up time (years)	Mean $\pm$ Std	3.3 $\pm$ 0.4	3.5 $\pm$ 0.5
	Median	3.2	3.4
	Range	2.6 – 4.3	2.3 – 5.0

Table 6. Long-Term Toxicities Present at Followup Visit

Variable	EBX	MMS
Number of Lesions (%)	208	208
No changes, relatively invisible scar	138 (66.7%)	143 (68.8%)
Late toxicities:		
Hyperpigmentation	124 (59.6%)	109 (52.4%)
Hyperpigmentation	11 (5.3%)	4 (1.9%)
Erythematous scar	6 (2.9%)	15 (7.2%)
Telangiectasia	65 (31.4%)	23 (11.1%)
Hair loss	8 (3.9%)	7 (3.4%)
Fibrosis	3 (1.4%)	2 (1.0%)
Atrophy	12 (5.8%)	9 (4.3%)
Loss of subcutaneous tissue	7 (3.4%)	6 (2.9%)
hypertrophy (excessive fibrosis) or Keloid	0 (0.0%)	3 (1.4%)
Poor healing, ulceration, erosion	4 (1.9%)	0 (0.0%)

EBX=electronic brachytherapy; MMS=Mohs micrographic surgery

Table 7. Secondary Endpoint: Cosmesis Grade at Follow-up Visit

Variable	EBX	MMS	
Number of Lesions (%)	208	208	
Clinician Cosmetic Grade Excellent/Good	203 (97.6%)	199 (95.7%)	
95% CI:	94.5% - 99.2%	92.0% - 98.0%	
p-value ( $\chi^2$ test):	0.277		
Clinician Cosmesis Grade <sup>1</sup>	Excellent	133 (63.9%)	142 (68.3%)
	Good	70 (33.7%)	57 (27.4%)
	Fair	1 (0.5%)	9 (4.3%)
	Poor	4 (1.9%)	0 (0.0%)
Subject Cosmesis Grade <sup>2</sup>	Excellent	140 (67.3%)	148 (71.1%)
	Good	48 (23.1%)	50 (24.0%)
	Fair	15 (7.2%)	10 (4.8%)
	Poor	5 (2.4%)	0 (0.0%)

( $\chi^2$  p-value = 0.277). Cosmesis ratings by patients were "excellent" or "good" in 90% of EBX-treated sites and 95% of MMS-treated sites  
1. Adapted from Cox et al.