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CyberKnife Stereotactic Accelerated Partial Breast Irradiation (CK-SAPBI)-Registry

Olusola Obayomi-Davies M.D. Principal Investigator

Department of Radiation Medicine

Georgetown University Hospital

3800 Reservoir Rd NW

Washington, DC 20008

P: 202-444-3320

F: 202-444-9323

Olusola.Obayomi-Davies@gunet.georgetown.edu

Brian T. Collins M.D. Study Chair

Department of Radiation Medicine

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1.0 SUMMARY

This observational registry trial will evaluate the efficacy and toxicity of Stereotactic Accelerated Partial Breast Irradiation (SAPBI) delivered with the CyberKnife in early stage breast cancer. We will evaluate oncologic and cosmetic outcomes.

Radiosurgery is defined as the stereotactic delivery of ionizing radiation in 5 days or less to a designated target with sub-millimeter accuracy. Radiosurgery in the context of this registry will be given to the region of the tumor bed within 12 weeks of breast conserving surgery or re-excision over a period of five to ten days using the CyberKnife (CK) with synchrony tracking.

This study will accrue 200 subjects over a two year period.

2.0 CLINICAL BACKGROUND

Breast conserving therapy is the preferred treatment approach for early stage breast cancer (1). Numerous randomized controlled studies have demonstrated equivalent overall survival for patients receiving breast conserving surgery with whole breast radiotherapy (WBI) compared with patients treated by mastectomy alone (2-8). The major advantage of breast conserving therapy (BCT) is the reduced psychological trauma associated with this process relative to mastectomy. The principal disadvantage of traditional breast conserving treatment is the prolonged daily radiation duration (~6 weeks), which may pose a prohibitive burden to patients.

Without adjuvant radiation therapy, the pattern of recurrence is overwhelmingly around the tumor bed (2-13). Sixty-five to 100% of breast recurrences reported after conservative surgery and whole breast radiation therapy have been found in the same quadrant as the initial tumor, with histology similar to the primary tumor, indicating that these recurrences probably represent residual viable cancer around the original site not eradicated by radiation therapy (14-17).

When the serial section mastectomy series by Holland that originally suggested high rates of multicentricity is re-analyzed with inclusion of only those cases with complete mammographic data and excluding those with evidence of microcalcifications or tumor density beyond the main tumor mass and unfavorable characteristics such as lobular histology, primary tumor larger than 2 cm, and cancer in the region 1 - 2 cm beyond the main tumor mass, only 4 of 72 cases had residual carcinoma more than 1 cm beyond the dominant mass (the area that would be treated with PBI) (18). Furthermore, breast recurrences distant from the primary site tend to occur later than those near the lumpectomy bed, and may well represent second primaries rather than true recurrences, which would not be expected to be prevented by whole breast radiotherapy (15).

From these data, one can infer that in appropriately selected cases, the main effect of radiation therapy following conservative surgery is the reduction of breast cancer recurrence at or very near the primary site. If radiation therapy is directed only to the tissue surrounding the excision cavity, then the entire course of radiation therapy can be accelerated markedly reducing

treatment time. Furthermore, normal tissues such as the remainder of the breast, underlying muscle, ribs, lung, and heart are generally spared with PBI, potentially avoiding toxicity.

There is a large body of mature Phase I/II and preliminary Phase III data available exploring the replacement of WBI with accelerated partial breast irradiation, (aPBI) using a variety of techniques. For appropriately selected patients treated with modern techniques, the results are encouraging and the techniques have been shown to be safe, tolerable, and highly reproducible with outcomes similar to WBI. **Table 1** summarizes partial breast irradiation studies.

Institution	# Cases	Median F/U (mo)	Scheme (cGy)	Total Dose (cGy)	% Local Recurrence	Good/Excellent Cosmetic Results
HDR Brachytherapy Series						
Ochsner Clinic[28 29] New Orleans, Louisiana	26	75	400 x 8	3200	2[a]	75[a]
Royal Devon/Exeter Hospital, Exeter, England [30]	45	18	1000 x 2 700 x 4 600 x 6	2000 2800 3600	8.8	95
National Institute of Oncology, Budapest, Hungary Phase *II* Trial [31]	45	60	520 x 7 433 x 7	3640 3030	4.4	97
National Institute of Oncology, Budapest, Hungary Phase III [31]	221	30	520 x 7 (HDR) 200 x 25[b] (EBRT)	3640 5000	0 < l	not stated Not stated
London Regional Cancer Center London, Ontario [32]	39	20	372 x 10	3720	2.6[a]	Not stated
William Beaumont Hospital [33,34]	79	52	400 x 8	3200	l	100
Radiation Therapy Oncology Group [35 36]	66	32	340 x 10	3400	n __	__ n
MammoSite® (FDA approval trial)[37]	43	8	340 x 10	3400	0	97
Tufts-New England Medical Center[38]	32	33	340 x 10	3400	3	88
Medical College of Virginia/VCU[39] a	44	42			0	80
LDR Brachytherapy Series						
Massachusetts General Hospital[40]	48	23	50	5000-6000	0	92
External Beam Radiotherapy Series						
Christie Hospital, Manchester, England [41 42]	353	65	500-531 x 8	4000-4200	25[d]	---
William Beaumont Hospital [43]	22	20	340-385 x 10	3400-3850	0	100
New York University [44]	47	18	600 x 5	3000	0	all late tox <=Gr 1
Florence Phase III [45]	520 (260)	60	600 x 5	3000	1.5%	90%

a = LDR/HDR patients combined
b = Whole breast irradiation
d = Eight year rate
HDR = High dose rate brachytherapy
LDR = Low dose rate brachytherapy
EBRT = External beam radiation

2.1 FRACTIONATION REGIMEN

The fractionation scheme of 30 Gy in five 6 Gy fractions used at NYU provides the basis for the adopted CyberKnife SAPBI regimen. 100 patients received 3D conformal aPBI with two tangential fields. With a median follow-up of 64 months, only 1 patient experienced a local recurrence (1% IBTR) (16). No patients experienced breast cancer related mortality and 89% of patients had good/excellent cosmesis. This fractionation scheme was also used in the PBI arm of a randomized controlled phase III trial of 520 patients with 5 years median follow-up. 1 patient in the partial breast arm experienced local recurrence compared to 3 patients in the WBI arm (45). In this trial up to 90% of patients experienced excellent/good cosmesis favoring the PBI arm.

The linear quadratic model and the BED equation $BED = (nd)(1+d/\alpha/ß)$ can be used to calculate isoeffective fractionation schemes where n is the number of fractions and d is the dose/fraction. From this equation, 30 Gy in 5 fractions of 6 Gy should be radiobiologically equivalent to 50 Gy in 25 fractions if the α/ß for tumor control = 4 Gy (17). A recently published randomized trial of 1410 patients suggests that α/ß for late normal tissue change in the breast = 3.6 Gy (18) and α/ß for breast cancer = 4.0. (19)

2.2 CYBERKNIFE BACKGROUND

CyberKnife is a treatment planning, imaging, and delivery system for image-guided stereotactic radiosurgery that was approved in 2001 by the U.S. FDA for treatment of lesions anywhere in the body. The imaging system provides real-time, orthogonal x-ray images of the patient to verify treatment position and alignment. Computers provide tracking of implanted fiducials along the x, y, and z-axes and rotations about each axis. Dynamic tracking data are then automatically transmitted for positioning and pointing of the compact 6MV linear accelerator mounted on a robotic arm that can deliver multiple, non-isocentric, non-coplanar radiation beams.

Synchrony is a CyberKnife motion tracking system that provides dynamic image guidance of targets that move under the influence of respiration. Before the start of treatment, Synchrony software builds a 3-dimensional model of chest wall movement and target motion during respiration. The model is continuously updated during treatment with live orthogonal x-ray images and provides real time data to compensate for target motion during respiration.

The target acquisition and tracking capabilities of the CyberKnife system should eliminate much of the uncertainty of target position present in conventional 3-D Conformal PBI, and thus should eliminate the need to expand treatment volume, reducing radiation exposure to normal tissue. In a dosimetric study comparing PBI with CyberKnife in 14 patients with intensity-modulated radiation therapy (IMRT) and 3-D conformal RT techniques in the published literature demonstrated improvement in coverage while minimizing dose to the normal breast with CyberKnife (20). In this analysis, the coverage of the PTV was the highest with CyberKnife.

Moreover, the ratio of V20 to V100, reflecting the conformity of the treatment was the lowest with CyberKnife planning.

Compared to existing existing PBI techniques, we expect once-daily CK-SAPBI to be more convenient for postmenopausal patients than twice-daily MammoSite or 3-D conformal PBI. There are other unique advantages to CyberKnife PBI. The target tracking and respiratory motion management capabilities of the CyberKnife reduce setup uncertainty thus requiring smaller PTV expansions. This translates to smaller normal breast volumes receiving high dose irradiation.

CyberKnife requires no implanted catheter(s), thus eliminating the need for a 2nd surgical procedure and reducing the risk of infection. There will be fewer technical limitations with CyberKnife compared to MammoSite related to minimum skin spacing and conformation of a balloon catheter to the lumpectomy bed. Considerably less normal tissue will be treated to high dose than with 3-D Conformal PBI given the CyberKnife's sub-millimeter accuracy. **Table 2** summarizes the CK-SAPBI experience.

Institution	# Cases	Median F/U (Weeks)	Scheme (cGy/# of Fx)	Total Dose (cGy)	% Local Recurrence	Cosmesis (%) (Good/Excellent)
GUH [24]	10	56	600 x 5	3000	0	100
Swedish [25]	9	28	600 x 5 340 x 10	3000 3400	0	100
UTSW [26]	45	100	600 x 5 625 x 5 700 x 5	3000 3250 3500	0	93-100
Swedish/Winthrop [27]	47	124	600 x 5 340 x 10	3000 3400	0	100

Table 2. Summary of CK-SAPBI studies

3.0 STUDY AIMS

Primary Aim: To evaluate the in-breast local failure (Ipsilateral breast events) and patterns of in-breast failure following CK-SAPBI.

Secondary Aim: To evaluate the oncologic outcomes, local toxicity and cosmetic outcomes following CK-SAPBI.

4.0 ENDPOINTS

Primary Endpoint: The primary endpoint for this study is the percentage of enrolled subjects who experience an ipsilateral breast recurrence. Ipsilateral breast recurrence is defined as time from end of radiation treatment to recurrence of disease in the breast.

Secondary Endpoints:

- Contralateral breast recurrence defined as time from end of radiation treatment to diagnosis of disease in the contralateral breast
- Regional recurrence free interval defined as time from end of radiation treatment to the diagnosis of disease in the regional lymph nodes.
- Distant disease free interval defined as the time from end of radiation treatment to first diagnosis of distant disease, regardless of the occurrence of any intervening local or regional failure, contralateral breast cancer, or non-breast second primary cancer.
- Mastectomy free survival defined as time from end of radiation treatment to mastectomy, death, or last follow-up.
- Recurrence-free survival defined as the time from end of radiation treatment to first diagnosis of a local, regional, distant recurrence, or death, regardless of any intervening contralateral or other second primary cancer.
- Overall survival defined as the time from end of radiation treatment to death due to any cause.
- Treatment related toxicity based on CTCAE version 4.0
- Treatment related Cosmesis based on the Harvard Cosmesis Scale

Assessment Time points: Assessments will be completed following CK-SAPBI at 4 weeks, 3 months, 6 months, 12 months, 18 months, 24 months, 3 years, 4 years and 5 year time points.

5.0 PATIENT ELIGIBILITY AND INELIGIBILITY CRITERIA

5.1 Inclusion Criteria

Subjects are eligible to participate in the registry if they receive CK-SAPBI in 5 fractions within 12 weeks of surgery and sign an institution specific consent form.

Additionally, subjects will be considered standard risk and optimal for CK-SAPBI if they meet the following criteria:

-Newly diagnosed AJCC (seventh edition) Stage 0 or I breast cancer.
-On histological examination, the tumor must be DCIS or invasive non-lobular carcinoma of the breast
-Surgical treatment of the breast must have been wide excision, lumpectomy or partial mastectomy
-Age 50 years or greater
-ER positive
-PR positive
-Her2 negative (IHC 0-1+; for IHC 2+, FISH must be non-amplified)
-Subjects with invasive tumors should undergo axillary sentinel lymph node evaluation or axillary lymph node dissection.
-Negative inked surgical margins of excision or re-excision, clear of invasive tumor and DCIS by at least 2 mm
-Negative post-excision or post-reexcision mammography if cancer presented with malignancy-associated microcalcifications with no remaining suspicious calcifications in the breast before radiotherapy. Alternatively, a specimen radiograph can be obtained showing all the suspicious calcifications.
-No involved axillary lymph nodes, N0(i+) allowed
-Target lumpectomy cavity/whole breast reference volume must be <30% based on treatment planning CT

Subjects not meeting above criteria but not expressly excluded in section 5.2 can be included in registry but will analyzed separately as a high risk cohort.

5.2 Exclusion Criteria

Subjects will be ineligible for CK-SAPBI and excluded from the registry inclusion if they meet any of the following criteria:

-Patients with invasive lobular carcinoma or nonepithelial breast malignancies such as sarcoma or lymphoma.
-Patients with tumors greater than 2 cm
-Patients with surgical margins which cannot be microscopically assessed or not cleared by at least 2mm at pathological evaluation.
-Patients with multicentric carcinoma or with other clinically or radiographically suspicious areas in the ipsilateral breast unless confirmed to be negative for malignancy by biopsy. Breast MRI will be required to exclude multicentric disease and additional suspicious areas will require biopsy to exclude malignancy.
-Patients with involved axillary nodes.
-Patients with collagen vascular diseases (active).
-Patient with known deleterious BRCA1/2 mutations or known mutations in other high penetrance genes (TP53, STK11, PTEN, CDH1)
-Patients with prior ipsilateral breast irradiation.
-Patients with prior ipsilateral thoracic irradiation.
-Patients with Paget's disease of the nipple.
-Patients with diffuse suspicious microcalcifications.
-Patients with suspicious microcalcifications remaining on the post-excision mammogram.

-Patients receiving (neo)adjuvant systemic therapy other than hormonal therapy
-Patients with oncoplastic reconstruction and absence of surgical clips

6.0 TREATMENT GUIDELINES

6.1 Surgery and Fiducial Placement

All patients should undergo margin negative resection with breast conserving surgery. A negative margin is defined as a no tumor on ink for invasive disease and 2 mm or greater DCIS. A re-excision is allowed to clear margins. Surgical clips can be placed during surgery to assist in delineation of the lumpectomy cavity.

Four gold fiducial markers will be placed in a manner that defines the superior, inferior, medial and lateral boundaries of the lumpectomy cavity and allows for optimal Synchrony tracking. Fiducial markers may be placed at time of re-excision or at a later time under image guidance if necessary. The markers should ideally be placed at least 2 cm apart and within 1 cm of the lumpectomy cavity. They should never be placed in the same axial plane, which could impair Synchrony tracking.

A recently available tissue marker, BioZorb® from Focalrx is a bioabsorbable 3D implant with 6 imbeded fiducials placed at the time of surgery uniquely delineates the surgical site of tissue removal in three dimensions provides a stable platform that facilitates 6-D tracking. BioZorb has been shown to reliably delineate the lumpectomy cavity and reduce the PTV boost size by as much as 50% with external beam radiation therapy. The BioZorb implant is the preferred tissue delineation marker and at Georgetown University Hospital.

6.2 Simulation

A contrast enhanced treatment planning CT scan with the patient in the supine position with her arms at her side will be required. The CT should start at or above the thyroid and extend several cm below the infra-mammary fold to include the entire lung. A CT slice thickness of 1-1.25 mm will be employed. Chin, shoulders and breasts should be included in the scan. The CT scan will be obtained with breath hold at end inspiration.

6.3 Contouring Target and Normal Structurtes

The following structures will be contoured in all cases: BioZorb implant/lumpectomy cavity, clinical target volume, planning target volume, skin, chest wall, ipsilateral lung, contralateral lung, thyroid, ipsilateral breast, contralateral breast and heart. Target structures and normal tissue structures should be outlined on all appropriate CT slices.

6.3.1 Lumpectomy Cavity - The lumpectomy cavity will be outlined based on visualization on CT and using surgical clips and post-operative changes when present. When a BioZorb implant is present, it can be outlined as a surrogate for the lumpectomy cavity

6.3.2 Clinical Target Volume (CTV)-The CTV will be defined uniformly by expanding the lumpectomy cavity by 5-15mm. The CTV will not extend beyond the skin, breast or into the chestwall.

6.3.3 Planning Target Volume (PTV) - The PTV will be defined by uniformly expanding the CTV by 0-5mm. The final PTV volume cannot exceed the lumpectomy plus a 20mm margin.

6.3.4 Skin - The skin is defined as 0 to 2 mm inside the external contour.

6.3.5 Chest wall - The chest wall includes the ribs, intercostal and pectoralis muscles.

6.3.6 Heart - The heart should be contoured beginning just below the level in which the pulmonary trunk branches into the left and right pulmonary arteries. The heart should be contoured on every contiguous slice to its inferior most extent near the diaphragm.

6.3.7 Lungs- The ipsilateral and contralateral lungs will be contoured separately.

6.3.8 Thyroid- All visible thyroid tissue will be contoured. If a thyroidectomy has been performed, this volume can be excluded.

6.3.9 Whole Breast-The whole breast will be defined as all breast volume expected to reside within the boundaries of standard tangential breast field excluding the lung and any non breast structure deep to the lung-rib interface such as heart, precardiac fat and liver. To facilitate reproducibility, external wires can be used to define the borders of all visible breast tissue during CT image acquisition.

6.4 CyberKnife Treatment Planning

Inverse planning using the CyberKnife software will be performed to yield a treatment plan. The treatment plan used for each individual case will be based on an analysis of the volumetric dose including dose-volume histogram (DVH) analyses of the PTV and critical normal structures. The number of paths and beams used for each patient will vary and will be determined by the selected treatment plan.

6.4.1 Dose Prescription - The total dose is 30.0 Gy, which will be delivered in five equal fractions of 6.0 Gy per day over 5-10 total days.

Quality assurance of dose distribution - Dose volume histogram (DVH) analysis confirms that the prescribed dose covers at least 95% of PTV.

6.4.2 Bolus -Bolus to improve anterior target coverage should not be used.

6.4.3 Synchrony- Synchrony must be used to track respiratory motion.

6.4.4 Dose limitations for normal tissues: Dose limitations will adhere to the ongoing guidelines as follows:

Uninvolved normal breast: Ideally, <50% of the whole breast reference volume should receive ≥ 50% of the prescribed dose and < 30% of the whole breast reference volume should receive the prescribed dose; V15Gy <50%, V30Gy<30%

Contralateral breast: The contralateral breast reference volume, contoured using the same methods described for the ipsilateral breast reference volume, should receive <3% of the prescribed dose to any point. Dmax< 0.9 Gy

Ipsilateral lung: <15% of the lung can receive 30% of the prescribed dose; V9Gy<15%

Contralateral lung: <15% of the lung can receive 5% of the prescribed dose; V1.5Gy < 15%.

Heart (right-sided lesions): <5% of the heart should receive 5% of the prescribed dose; V1.5Gy< 5%.

Heart (left-sided lesions): The volume of the heart receiving 5% of the prescribed dose should be less than the 40%; V1.5Gy< 40%,
Mean Heart Dose <3Gy

Thyroid: maximum point dose of 3% of the prescribed dose; Dmax <0.9 Gy

Skin: Maximum point dose < 36 Gy.

Chest Wall: Maximum point dose <36 Gy.

Critical normal tissue dose within 5% of the specified value for the breasts, lungs and heart will be considered acceptable (section 6.4.4).

7.0 PATIENT ASSESSMENT

Clinical examination and disease status assessment will be completed at 4-6 weeks, 6 months, 12 months, 18 months, 24 months and yearly intervals thereafter for five years.

At each patient assessment, the follow-up, cosmesis and disease progression case report forms must be completed.

7.1 Response Criteria-Treatment Failure

7.1.1 The definition of a treatment failure is radiographic evidence of recurrent carcinoma, confirmed by biopsy.

7.1.2 Ipsilateral in-breast recurrence: Defined as evidence of invasive or in situ breast cancer (except LCIS) in the ipsilateral breast. Patients who develop clinical evidence of tumor recurrence in the remainder of the ipsilateral breast must have a biopsy of the suspicious lesion to confirm the diagnosis with documentation of the location. For this analysis, ipsilateral in-breast recurrences will be further characterized as in-field (within the prescription isodose line) or marginal (outside the prescription isodose line but within the 95% prescription isodose line) and distant (beyond the 50% prescription isodose line).

7.1.3 Local chest wall recurrence: Defined as evidence of invasive or in situ breast cancer (except LCIS) in the ipsilateral chest wall. Patients who develop clinical evidence of tumor recurrence in the ipsilateral chest wall must have a biopsy of the suspicious lesion to confirm the diagnosis. These will be considered Ipsilateral-breast events.

7.1.4 Regional recurrence: Defined as the development of tumor in the ipsilateral internal mammary, ipsilateral supraclavicular, ipsilateral infraclavicular and/or ipsilateral axillary nodes confirmed by biopsy.

7.1.5 Distant recurrence: Defined as evidence of tumor in any area of the body, with the exception of those described in Sections 7.1.2, 7.1.3, and 7.1.4.

7.1.6 Contralateral Breast Event (CBE): Defined as evidence of invasive or in situ breast cancer (except LCIS) in the contralateral breast or chest wall. The diagnosis of a CBE must be confirmed histologically.

8.0 STATISTICAL CONSIDERATIONS

8.1 Endpoints

Primary Endpoint: The primary endpoint for this registry is the percentage of subjects that develop an ipsilateral breast event (IBE). IBEs will be sub-analyzed by histology.
Secondary Endpoints:
Oncologic outcomes sub-analyzed by histology.

- Contralateral breast recurrence defined as time from end of radiation treatment to diagnosis of disease in the contralateral breast.
- Regional recurrence free interval defined as time from end of radiation treatment to the diagnosis of disease in the regional lymph nodes.
- Distant disease free interval defined as the time from end of radiation treatment to first diagnosis of distant disease, regardless of the occurrence of any intervening local or regional failure
- Mastectomy free survival defined as time from end of radiation treatment to mastectomy, death, or last follow-up.

- Recurrence-free survival defined as the time from end of radiation treatment to first diagnosis of a local, regional, or distant recurrence, or death regardless of any intervening contralateral or other second primary cancer.
- Overall survival defined as the time from end of radiation treatment to death due to any cause.

Treatment related toxicity based on CTCAE version 4.0

Treatment related Cosmesis based on the Harvard Cosmesis Scale

8.2 Sample Size

200 subjects who opt for CK-SAPBI will be treated according to this protocol for consistency. It is expected that 200 subjects will enroll on the study over approximately 2 years.

8.3 Analysis Plan

Interim analyses will be performed at median follow-up of 12 months and 24 months. Final analyses will be completed at median follow-up of 60 months. A separate high risk outcomes analysis will be performed for subjects enrolled without meeting all the inclusion criteria.

8.3.1 Adverse events and complications will be tabulated by system affected according to CTCAE Criteria version 4. Rates will be reported with 95% exact binomial confidence intervals to be informally compared with those of conventional therapy.

8.3.2 Median time to ipsilateral breast recurrence, contralateral breast recurrence, regional recurrence, and distant recurrence will be estimated using the Kaplan-Meier method and reported with a 95% confidence interval. Subgroup-analysis will completed by histology.

8.3.3 Mastectomy-free survival, recurrence-free survival, and overall survival will be calculated using Kaplan-Meier estimates with 95% confidence interval.

8.3.4 Cosmesis measures will be reported as physician-scored cosmesis using the Harvard cosmesis scale.
8.3.5 Total treatment volume will be recorded for each patient. The mean, standard deviation, median, and range will be reported for informal comparison with conventional radiation therapy.

9.0 DATA USE AGREEMENT

See data use agreement.

10.0 REGSITRY PARTICIPATION

To participate in the registry, potential sites must submit their respective institution IRB applications. Once IRB approval is finalized, sites will forward a copy of the IRB approval and

Investigator Study Specific Disclosure Forms (SSDF) to Dr. Obayomi-Davies at Georgetown University Hospital and return a signed data use agreement. Once all documents are received, a registry access account will be created.

Up to two accounts for the principal investigator and a study coordinator can be created for each site. The principal investigator and coordinator may be the same individual.

10.1 Data Management

The registry data will be managed with Clinovo electronic data capture. A unique study ID will be assigned to each registry subject. Participating sites should maintain a master list with study-ID information and institutional specific identifiers which will not be disclosed. No specific identifying information will be shared with the registry.

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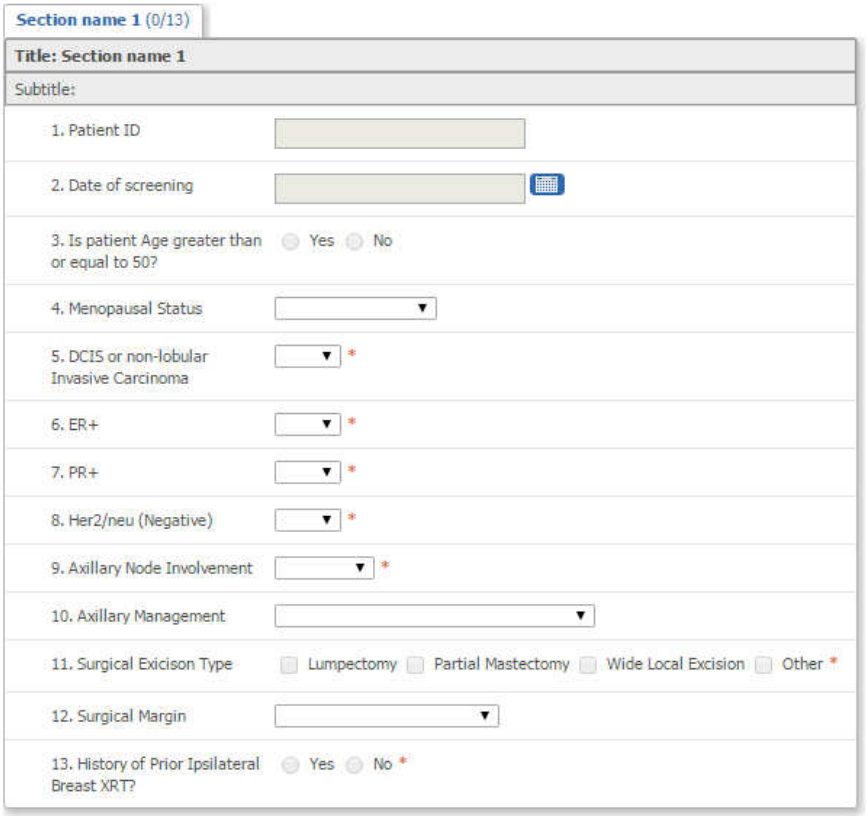
APPENDIX I-Consent Form (Attached)

APPENDIX II: CASE REPORT FORMS



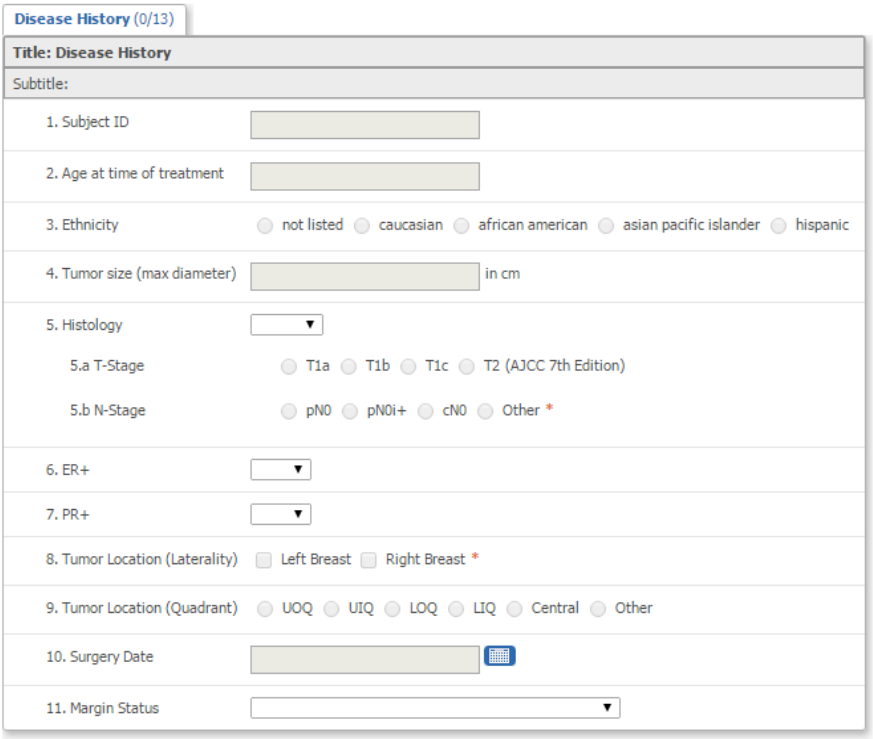
Section name 1 (0/13)

Title: Section name 1

Subtitle:

1. Patient ID
2. Date of screening
3. Is patient Age greater than or equal to 50? Yes No
4. Menopausal Status
5. DCIS or non-lobular Invasive Carcinoma *
6. ER+ *
7. PR+ *
8. Her2/neu (Negative) *
9. Axillary Node Involvement *
10. Axillary Management
11. Surgical Exicison Type Lumpectomy Partial Mastectomy Wide Local Excision Other *
12. Surgical Margin
13. History of Prior Ipsilateral Breast XRT? Yes No *

Screening



Disease History (0/13)

Title: Disease History

Subtitle:

1. Subject ID
2. Age at time of treatment
3. Ethnicity not listed caucasian african american asian pacific islander hispanic
4. Tumor size (max diameter) in cm
5. Histology
   - 5.a T-Stage T1a T1b T1c T2 (AJCC 7th Edition)
   - 5.b N-Stage pN0 pN0i+ cN0 Other *
6. ER+
7. PR+
8. Tumor Location (Laterality) Left Breast Right Breast *
9. Tumor Location (Quadrant) UOQ UIQ LOQ LIQ Central Other
10. Surgery Date
11. Margin Status

Disease History

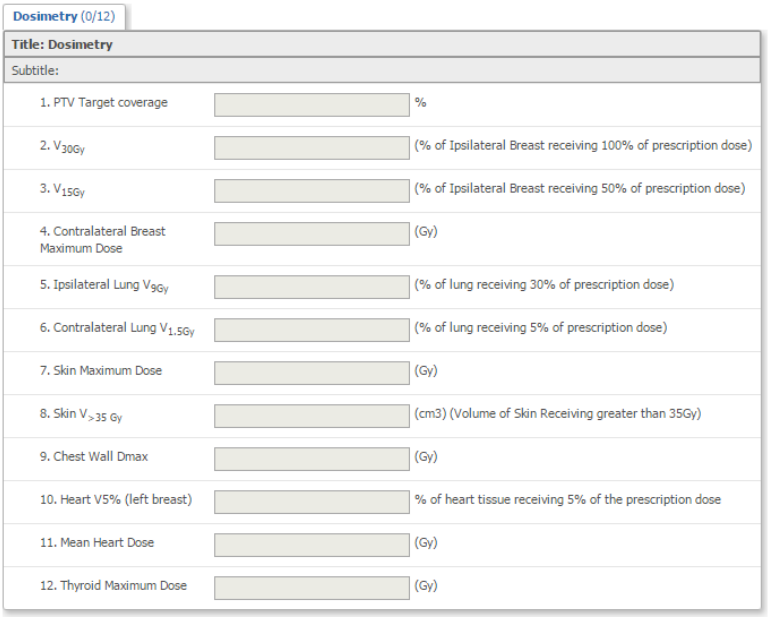
Treatment (0/14)

Title: Treatment

Subtitle:

1. Radiation Start Date	
2. Radiation Stop Date	
3. Last Follow-up date	
4. PTV (cm3)	
5. Prescription Dose	Gy
6. Number of Fractions	
7. Dose per fraction	Gy
8. Prescription Isodose Line	%
9. Number of Beams	
10. Treatment Time (minutes)	(Multiplan Estimated Treatment Time)
11. Fiducial Placement	*
12. Date Fiducials Placed	*
13. Number of Fiducials Placed	3 4 5 6 Other
14. Number of Fiducials Tracked	3 4 5 6 Other

Treatment Details



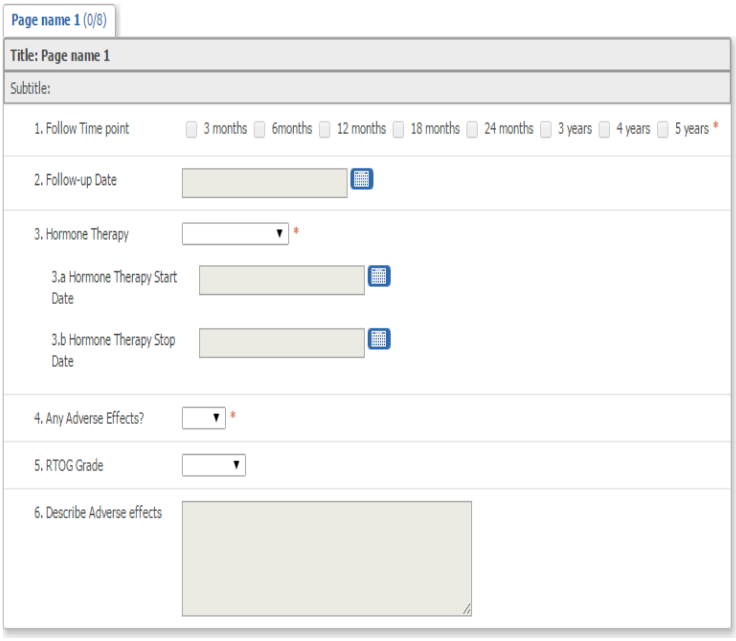
Dosimetry (0/12)

Title: Dosimetry

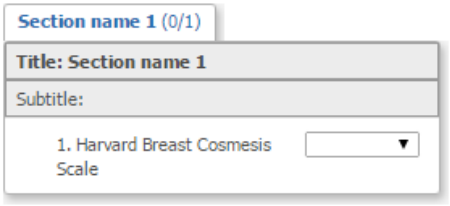
Subtitle:

1. PTV Target coverage	%
2. V_{30Gy}	(% of Ipsilateral Breast receiving 100% of prescription dose)
3. V_{15Gy}	(% of Ipsilateral Breast receiving 50% of prescription dose)
4. Contralateral Breast Maximum Dose	(Gy)
5. Ipsilateral Lung V_{9Gy}	(% of lung receiving 30% of prescription dose)
6. Contralateral Lung $V_{1.5Gy}$	(% of lung receiving 5% of prescription dose)
7. Skin Maximum Dose	(Gy)
8. Skin $V_{>35\ Gy}$	(cm3) (Volume of Skin Receiving greater than 35Gy)
9. Chest Wall Dmax	(Gy)
10. Heart V5% (left breast)	% of heart tissue receiving 5% of the prescription dose
11. Mean Heart Dose	(Gy)
12. Thyroid Maximum Dose	(Gy)

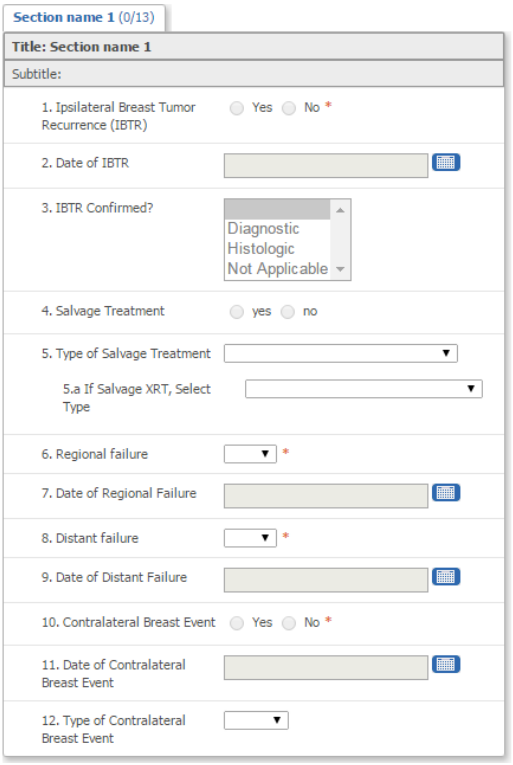
Radiation Dosimetry



Follow-up



Cosmesis



Disease Progression

APPENDIX 3: DATA USE AGREEMENT