BABEŞ-BOLYAI UNIVERSITY

CLUJ-NAPOCA

FACULTY OF ENVIRONMENTAL SCIENCE AND ENGINEERING

Dosimetric and quality assurance procedure evaluation of the strut-adjusted SAVI hybrid device used in accelerated partial breast irradiation

- Summary of DOCTORAL THESIS –

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CHAPTER 1 INTRODUCTION

Cancer is considered nowadays as being one of the most aggressive large groups of diseases that can affect the normal functionality of any part or organ the human body, due to its ability to grow and spread uncontrolled. Breast cancer is among the most common cancer in women in the world, and the most common in women in USA.

Treatment of breast cancer can be a combination of local management and systemic treatment. Most breast cancer patients are treated with both using local and systemic treatment regimens. When radiation therapy is the sole and primary treatment option, the excision of the tumor is usually followed by a course of radiation therapy, which can be 1) external or 2) internal (brachytherapy), meant to remove residual microscopic disease. This is a conservative treatment modality, since it conserves the breast, decreases the chance of recurrence and eradicates the residual tumor. Various irradiation techniques, traditional or novel, are available and can be employed (Devlin *et al*., 2016; Baglan *et al*., 2001; Benitez *et al*., 2004; Mooij *et al*., 2014).

The **research objective** of this thesis is to quantify the dosimetric performance and to evaluate quality assurance procedures for a device specifically designed for *Accelerated Partial Breast Irradiation* (APBI) treatment of early stage breast cancer patients by means of High Dose Rate brachytherapy, namely the Strut Adjusted Volume Implant (SAVI) applicator (Cianna Medical, Aliso Viejo, CA).

Our research is a comprehensive dosimetric evaluation and analysis of various coverage parameters, and doses to adjacent critical structures have been estimated in all patients included in a retrospective study encompassing more than five years of cumulated clinical data. Proposed improved guidelines for daily treatment clinical QA and workflow are also presented and discussed.

The following major objectives of the study were achieved:

1) Using an extensive multi-institutional and single-institution clinical data, collected for all four different size SAVI devices (SAVI6-1mini, SAVI6-1, SAVI8-1 and SAVI10-1) to presents the dosimetric analysis of the entire range of SAVI applicators and specifically for the smallest size SAVI6-1mini device.
2) Performing intercomparison studies among different APBI devices, which allowed us to highlight the various dosimetrical advantages of the SAVI device over the balloon type APBI devices.
3) Outlining the frame of a comprehensive and experience driven and tested quality assurance program that must be implemented in order to properly design the workflow and address the complexities of a busy partial breast brachytherapy department.
4) Successfully establishing such an HDR partial breast brachytherapy program in our clinical practice, at Texas Oncology Denton, Texas, USA.

Certain **specific objectives** were planned for:

1) The dosimetric analysis and characterization of all available SAVI devices;
2) The use of other available partial breast brachytherapy devices, FDA approved in USA, in order to compare their performances in given clinical situations;
3) Evaluating Conformity Indexes (CI), related to reported air/seroma and invagination volumes, in view of proposed values in national protocols;
4) All dosimetric data, both the major pool and minor subset, was stratified using 5 mm skin-bridge intervals, therefore differentiating among cases with major or no PTV volume reduction.
5) Evaluating the impact of heterogeneities on standard calculated and reported coverage parameters, by means of using a novel computational algorithm, ACUROS Brachyvision (Varian Medical Systems, Palo Alto, CA);
6) Participating in a 5 year retrospective study on all SAVI device types (Yashar *et al*., 2016), and reporting the results in terms of local control, toxicity, and survival for the first 250 patients treated across multiple institutions, which included our own.

The current thesis is structured in eight chapters, a short description of each being presented in the following paragraphs. The thesis is structured in two main bodies of work: a theoretical section that discusses fundamental physical and anatomical concepts, and

surveys the treatment modalities currently available for breast cancer, and an empirical and experimental section in which original contributions are discussed.

As such, the first section of the thesis is comprised of four chapters:

Chapter 2 – Theoretical Aspects, is a review of the fundamental theoretical concepts and quantities used to describe the interactions of ionizing radiation, both gamma and x-ray, with matter, and the methods used to measure those quantities, with an emphasis on the kinematics and probability of the Compton interactions.

Chapter 3 – Brachytherapy, overviews general aspects of High Dose Rate Brachytherapy, with special attention given to the standard TG43 dose calculation formalism and the ACUROS BV novel algorithm used in brachytherapy computations.

Chapter 4 – Overview of breast cancer treatment modalities, presents the treatment modalities currently available for breast cancer, with an emphasis on the brachytherapeutical options.

The next chapters include our original contributions and results:

Chapter 5 – Dosimetrical evaluation of a strut-adjusted-volume-implant SAVI device used for APBI, presents the framework of our study, in which we describe the physical characteristics of the SAVI device, the patient selection criteria, and we clarify the main dosimetric parameters used in evaluating the performance of this device. We also present our comparison study against balloon type devices, MammoSite versus Contura.

Chapter 6 – Comprehensive dosimetric analysis of the SAVI device, is the main body of our work consisting of a comprehensive dosimetric analysis of extensive clinical data, collected for all four different size SAVI devices (SAVI6-1mini, SAVI6-1, SAVI8-1 and SAVI10-1). The total number of patients included in our multi-institutional pool study was 817, from 14 different participating, each providing data for all four SAVI device models. The subset study presented on the SAVI6-1mini device is a single-institution study of plans created for 121 patients, treated over the span of 5 years, from 2009 to 2014.

Chapter 7 - Comprehensive evaluation of a strut-adjusted-volume-implant SAVI device Quality Assurance Program, presents our own contribution to designing a comprehensive quality assurance program that deals with all stages of an APBI treatment

process in a busy radiotherapy department. We bring to light all possible un-common clinical situations, we highlight the common practices and the extra measures we included into our customized QA program, in an attempt to incorporate those into a comprehensive QA program capable dealing with even the least frequent clinical situations.

In **Chapter 8 – Clinical Results**, fhe final results and conclusions of this multi-layered study are corroborated with the results of a 5 year long clinical study we were part of, that confirms the validity of our dosimetrical study. This report also confirmed outstanding target coverage with excellent skin and rib sparing over the entire cohort of clinical data, and confirms excellent tumor control comparable to other published APBI rates and survival with low toxicity. Compared to external beam techniques for APBI, brachytherapy seems to be as effective, with less toxicity.

In the **Conclusions** chapter we present the general conclusions of our study, based on the our results and our original contributions.

CHAPTER 2 THEORETICAL ASPECTS

The radiations of primary concern for us are the ones originating in atomic and nuclear processes. Ionizing radiations are those radiations that can excite or ionize the atoms of the material they interact with. The International Commission on Radiation Units and Measurements (ICRU, 1971) makes a clear distinction between interactions of charged and uncharged particles, emphasizing the fact that there are two different mechanisms by which the process of ionization can take place: *directly* and *indirectly ionizing radiation.*

There are five different mechanisms by which the photons are interacting with matter: scattering, photoelectric effect, Compton effect, pair production and photo disintegration, respectively. Of those, the Compton effect is the dominant effect in the range of energies regularly dealt with in brachytherapy, therefore twe summarized important theoretical aspects of this physical phenomenon: kinematics and probability of Compton interaction.

The quantities describing the interaction of radiation with matter are also defined and discussed: 1) *Kerma, K*, a quantity that describes the energy transfer from indirectly ionizing radiations (photons) to charged particles, 2) the *Exposure, X*, a quantity that

describes gamma or X-ray beams in terms of their ability to ionize a volume of air, and 3) the *Absorbed Dose, D*, a quantity that describes the energy transfer from directly ionizing radiations to matter.

The calculation of dose in both external beam therapy and brachytherapy is a very complex process because of the complexity of factors that are to be taken into account. Only the fundamental factors were presented in this paper but many other are included in current dose calculation formalisms, especially because the evolvement of new technologies that were adopted into the clinical environment nowadays.

CHAPTER 3 BRACHYTHERAPY

Since the method of testing used in this project utilized High Dose Rate Brachytherapy (HDR), only the characteristics related to this method of treatment are presented.

The most popular and almost universally used dose calculation formalism today is TG43 (Raviner *et al*., 1994), a formalism used to establish the 2-D dose distribution around cylindrically symmetric sources. The distribution of the dose cloud around brachytherapy sources are generally computed by assuming only photon interactions, affected by the surroundings and the emitted radiation. The dose contribution at a certain point from a single source of finite dimensions is the sum of doses from multiple point sources. When free space is the medium for a given source, it is considered that there are scattering or absorption effects to be counted for, but absorption and scatter effects need to be considered at any point situated at some distance away from the source placed in a water medium.

Acuros BV is an algorithm that allows dose-to-medium distribution calculations, in addition to the standard dose-to-water calculations available in modern treatment planning systems using just the TG43 formalism. Specific to the Acuros BV is that it calculates dose distributions through solving the Linear Boltzmann Transport Equation (LBTE). The LBTE is the equation that describes the macroscopic behavior of radiation particles (neutrons, gamma-rays, electrons, etc.) as they travel through and interact with matter.

Although there are several advantages of HDR over LDR (Kubo *et al*., 1998), the biggest controversies over the two techniques of dose delivery, were related to the

radiobiological effects. Historically, the comparison between LDR and HDR was done by the application of the Linear Quadratic Model (L-Q model). In this model the biologically effective dose (Fowler *et al*, 1992) (BED) is expressed as:

$$BED = - (\ln S.F.) / \alpha = NRt [1 + G \times Rt / (\alpha/\beta)] - kT \quad \textbf{(3.1)}$$

For HDR treatments, where the time between fractions is long compared to the half-time for repair, and the fraction is short, time t is approaching zero, so in this case G equals unity. Several publications contrasted and compared the effects of LDR and HDR with respect to tumor control and late effects (Hall, 2000) and it was concluded that at least from radiobiological standpoints HDR can safely replace LDR if enough fractions are delivered and the total doses are reduced accordingly.

The high-dose rate remote afterloader used in our department (Figure 1) is a VariSource iX HDR afterloader (VARIAN Medical Systems, Inc., Palo Alto, CA

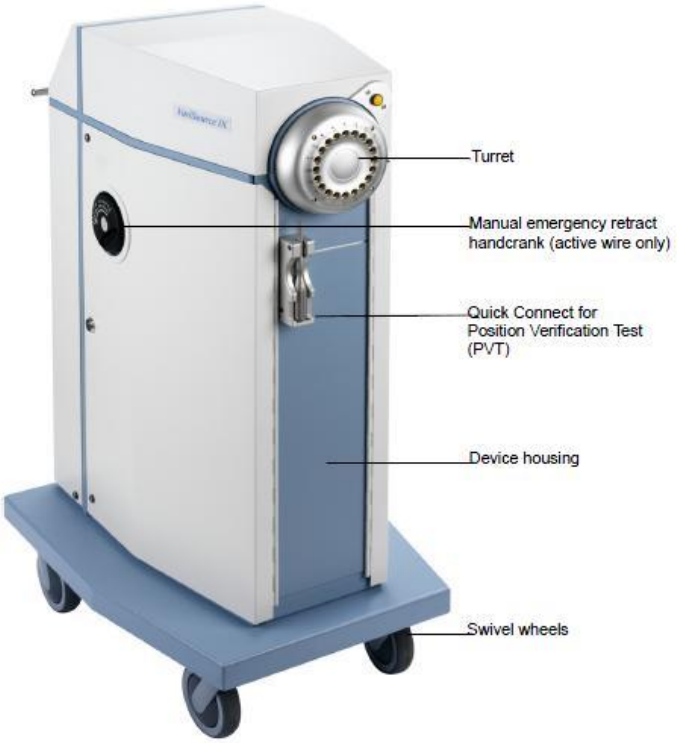


Figure 1. Depiction of a VariSource iX unit, with its main components

One of the most important tasks a Medical Physicist is required to perform is patient specific quality assurance (QA) (Khan, 2003). A robust quality assurance program is mandatory for the smooth operation of an HDR department. The HDR unit and console operation are tested prior to delivery of each treatment for safety interlocks, source decay and treatment time calculation (Kutcher, 1995).

Dose distribution analysis in the irradiated volume is most efficiently done using dose-volume histogram curves, since they allow individual patient plan evaluation and provide an excellent comparison tool for subsequent plans performed on the same CT data set (Gurdalli, 2008). DVHs allow for dose uniformity assessment, evaluation of the extent of hot spots in the irradiated volume, and greatly help in the plan optimization process.

CHAPTER 4 OVERVIEW OF BREAST CANCER TREATMENT MODALITIES

Breast anatomy is very important in order to understand the methods used in radiotherapy. The breast is made up of the mammary gland, fat, blood vessels, lymphatics and nerves (see Figure 2). The surface of the breast has deep attachments of fibrous septa which run between the superficial fascia attached to the skin and the deep fascia covering the pectoralis major and the other muscles of the chest wall.

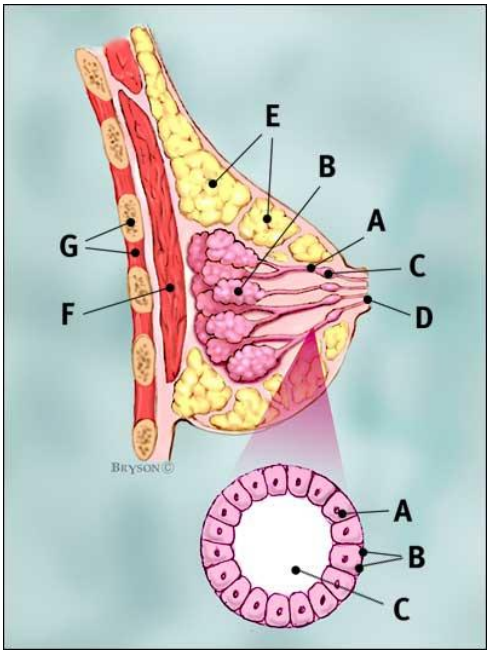


Figure 2. Breast anatomy**: A** ducts **B** lobules **C** dilated section of duct to hold milk **D** nipple **E** fat **F** pectoralis major muscle **G** chest wall/rib cage

The staging of breast cancer is actually related to the amount of tumor dissemination. Staging helps determining the best treatment available and estimates prognosis. The most widely used staging system for breast cancer, based on tumor size, number of lymph nodes involved and evidence of distant metastasis, is the TNM system developed by the American Joint Committee on Cancer. The most common histological type of breast cancer is infiltrating ductal carcinoma (~75%), followed by infiltrating lobular carcinoma (~10%), the rest consisting of other histological types.

The treatment of breast cancer can be a combination of local management and systemic treatment. When radiation therapy is employed, whole breast irradiation became a standard component of breast cancer therapy (Wazer *et al*., 2006). Certain disadvantages of external beam radiation therapy for breast cancer, mostly related to its relative complexity and related expenses, led to investigations done in the direction of HDR brachytherapy, and APBI.

Historically, partial breast irradiation was initially performed with interstitial implantation using multi-catheter brachytherapy. The simplicity of the single catheter insertion and the ability of the multi-catheter implants to adapt the dose distribution to the target was eventually achieved by the development of a new set of applicators, variation of the MammoSite balloon prototype, such as Contura^{TM} Multilumen Balloon (MLB) - SenoRx, Aliso Viejo, CA, a hybrid design, with several catheters enclosed in a balloon, and another novel device, the device we investigated in this study, the **SAVI** APBI device (Cianna Medical, Aliso Viejo, CA, USA).

Figure 3. The SAVI device (SAVI6-1mini, in this picture)

Since 2005, the year the NSABP B-39/RTOG 0413 breast national protocol was initiated and used, there have been three FDA (Federal Drug Administration – the official

regulatory entity of medical devices use in USA) approved single-entry multi-lumen intracavitary devices that have been introduced to the market: the MammoSite Single and Multi-Lumen device, the Contura Multi-Lumen (four different lumens) Balloon device, and the SAVI (Strut-Adjusted Volume Implant), the most recent device, which, on its largest model, can have up to 11 lumens (Figure 3).

Our center was one of the first stand-alone clinics in United States that published clinical research studies pertaining to the newly adopted PBI SAVI device (**Morcovescu *et. al*,** 2009), shortly after the initiation of its usage in our clinic. Our own experience with planning and treating SAVI patients is unique, and it comprises of more than 400 SAVI patients treated since the adoption of the SAVI device in our radiation department at Texas Oncology Denton. This translates in roughly these average numbers: 40+ SAVI patients/year, ~ 4 SAVI patients/ month, or 1 SAVI patient every week, since the very first case, in mid-2008.

The following Table 1 will be relevant about the trend of APBI devices usage in our department in the last 11 years, since 2006.

Table 1. Number of APBI cases treated at Texas Oncology Denton between 2006 and 2017, distributed per calendar year and per type of APBI device used (* - 1st SAVI case done in June, so # of cases accumulated until the end of 2008; ** - # of cases done until end of June, 2017)

		Year											
		2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Device type	MM_{sl}	30	28	16	5	1	0	0	0	0	0	0	0
	MM_{ml}	0	0	0	0	1	0	0	0	0	0	0	0
	Contura	0	3	24	3	0	0	0	0	0	0	0	0
	SAVI	0	0	20*	39	33	43	44	46	30	50	60	30**

Tabel 1 clearly shows the fact that while in 2006 only the MammoSite single lumen (MM_{sl}) device was used, due to unavailability of other APBI devices, the year of 2007 marked the slow and steady adoption of multi-lumen devices, i.e., the Contura device. We started using the SAVI device in June of 2008, and only one year later the profile of our HDR APBI program changed dramatically, significantly driven towards the use of multi-lumen devices (with only one use of the upgraded balloon type device, the multi-lumen MammoSite, MM_{ml}), favored over the use of the single-lumen MammoSite balloon.

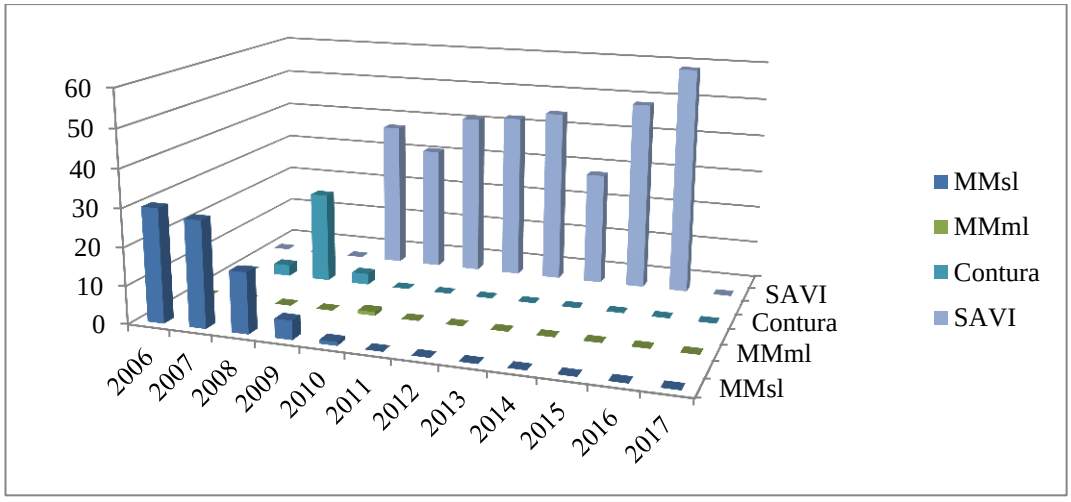


Figure 4. The SAVI device was fully adopted in 2009, and is the only APBI device used in our clinic from 2011 until end of June, 2017

The year of 2011 marked the full abandonment of this original single-lumen device and the full adoption of the use of the SAVI type devices for all our APBI patients, a steady trend in the last seven (7) years of our practice, much better visualized in Figure 4 above. This trend and evolution is extremely relevant, since it reveals the fact that the use of SAVI devices was easily embraced by the breast surgeon practice, adapted to their and our workflow, and overwhelmingly elected as the device of choice because of the positive cosmetic and clinical outcomes, reflective of the highly effective design of the device, which allowed for better dosimetrical optimization and adaptability to difficult clinical situations (reduced chest-wall and/or skin to lumpectomy cavity distances, due to small breasts or lumpectomy localization in the breast).

CHAPTER 5 DOSIMETRICAL EVALUATION OF A STRUT-ADJUSTED-VOLUME-IMPLANT SAVI DEVICE USED FOR ACCELERATED PARTIAL BREAST IRRADIATION

5.1 Device description

The SAVI (Strut-Adjusted-Volume Implant) device is a multi-catheter, single entry device manufactured by Cianna Medical, Aliso Viejo, CA, USA, that received 510(k) clearance in July 2006. The first preliminary scientific papers eventually including the SAVI device as a treatment option on their studies concerning accelerated partial breast irradiation were eventually first accepted and published no sooner than early of 2009

(Yashar *et al*., 2009), with publication of first clinical follow-up studies shortly thereafter (Yashar *et al*, 2009; Yashar *et. al*, 2011). The Texas Cancer Center clinic, where the candidate functions as a solo Physicist since late 2003, was the first SAVI treatment site in Texas, and among the firsts in the US, in November of the year 2008.

The device is shown in Figure 5 in both expanded (post-insertion) and collapsed (pre-insertion) format. The SAVI device comes in four different sizes, as displayed in Figure 6.

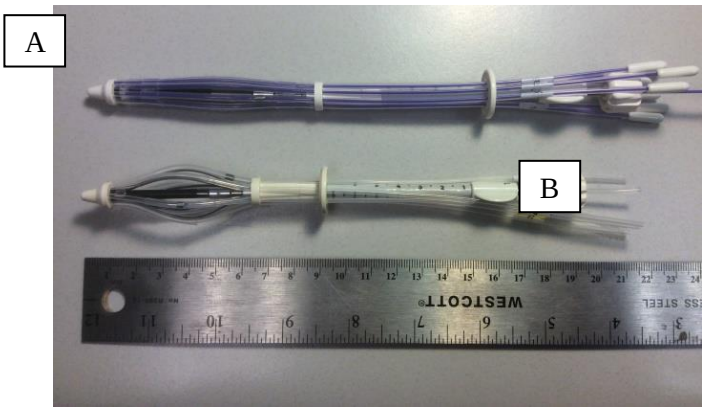


Figure 5. The SAVI device: A) collapsed and B) fully expanded

The major advantage of the SAVI device is patient-specific dose optimization from the multiple dwell positions in each strut to minimize dose to normal tissues, including skin, chest wall, and lung.

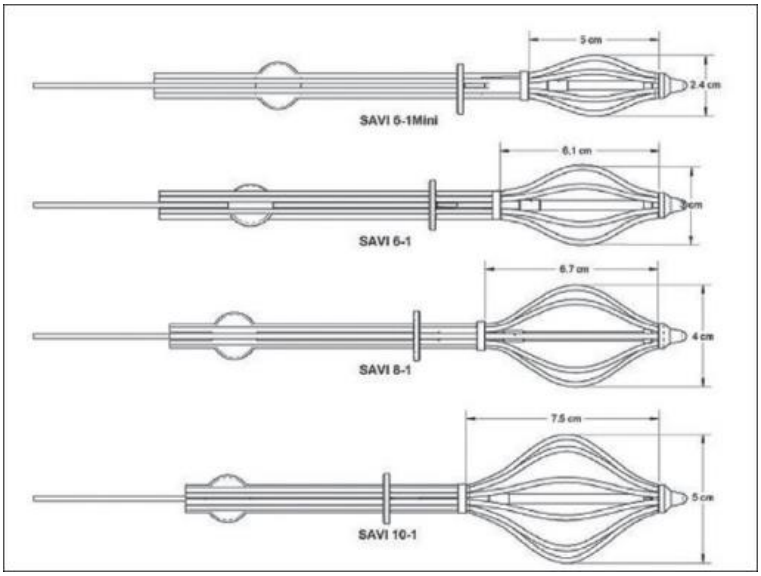


Figure 6. SAVI applicator sizes: 6-1Mini (top), 6-1, 8-1 and 10-1 (bottom)

Patient eligibility criteria for a SAVI implant verify those currently and widely accepted and employed in the industry, and in compliance with American Brachytherapy Society (ABS) and American Society of Breast Surgeons (ASBS) guidelines and the ASTRO consensus statement. As a rule, only patients with invasive breast cancer or ductal carcinoma *in situ*, stage 0, I or II breast cancer resected by lumpectomy, up to 3 cm tumor size, and excised with negative lymph nodes involvement, age ≥ 45 years, were accepted.

In order to evaluate the dosimetric features of the four (4) different SAVI devices subtypes described in the previous section, the following equipment was used: an 8 slice GE LightSpeed helical multislice CT Scanner and a Varian BrachyVision Treatment Planning System – Brachytherapy Planning Software (Version 13.6).

As emphasized in many publications on breast brachytherapy (Arthur *et al*., 2003; Patel et al., 2007; Hong *et al*., 2012; Mooney et al., 2015), dose volume histogram evaluation is the standard method of dosimetric plan characterization, usually used to determine the reliability of an implant, as eventually reflected in skin and normal tissue toxicity. Therefore we used the following prescribing, optimizing and reporting indices in this study:

- Rx Dose – prescribed dose, expressed in cGy.
- PTV – Ideal Planning Target Volume. This is the intended treatment volume (cubic centimeters).
- PTV_EVAL – Adjusted Planning Target Volume. This is the actually treatment volume used for optimization and coverage evaluation (cubic centimeters).
- Isodose Curve – A geometric curve graphically documenting all the points that receive an equal radiation dose.
- DVH - Dose-Volume Histogram. A plot of a cumulative dose-volume frequency distribution that graphically summarizes the simulated radiation distribution within a volume of interest of a patient that would result from a proposed radiation treatment plan.
- Coverage index (CI) - a measure of the fraction of the target volume receiving a dose equal to or greater to the prescribed dose, i.e. V100 expressed as a percent.
- V100 - Volume of tissue receiving at least 100% of the prescribed dose, expressed in absolute terms (cubic centimeters).
- V95 - Volume of tissue receiving at least 95% of the prescribed dose, expressed as a percentage of the total target volume.
- V90 - Volume of tissue receiving at least 90% of the prescribed dose, as a percentage of the total target volume.
- D90 - the percentage of the prescribed dose delivered to 90% of the PTV.

- V150 – the volume of tissue receiving at least 150% of the prescribed dose, expressed in absolute terms (cc's).
- V200 – the volume of tissue receiving at least 200% of the prescribed dose, expressed in absolute terms (cc's).
- Max Skin Dose – the maximum dose as calculated by the DVH in the Max Skin structure, expressed in absolute terms (cGy) or in relative terms (as a percentage of the prescribed dose).
- Max Chest-Wall/Rib Dose – the maximum dose as calculated by the DVH in the Max Chest-Wall or Rib structure, expressed in absolute terms (cGy) or in relative terms (as a percentage of the prescribed dose).
- DHI – dose homogeneity index, which is the equivalent to the fraction of the total treatment volume which receives a dose between 100% and 150% of the Rx dose

Treatment planning is usually more time consuming than for a typical MammoSite balloon applicator, but planning times are not prohibitive as standard template plans are created for each of the SAVI device types. Standardization of created APBI SAVI cavities was later adopted by others (Dahl *et al*., 2014), since it improves consistency of SAVI cavity reconstruction. This allows for quick digitization and reconstruction of the multiple struts. The lumpectomy or SAVI cavity is defined by the physician, as this becomes the reference structure from which all planning target volumes are eventually obtained.

The library of created structures was created based and following closely on the recommendations of the NSABP B-39/Radiation Therapy Oncology Group 0413 protocol, and included: the *Planning Target Volume* (PTV) is generated by a 1 cm uniform expansion of the lumpectomy cavity volume, and it is defined as the difference between the expanded volume and the cavity volume, the *Planning Target Volume for Evaluation* (PTV_EVAL), the same as the PTV but limited to 5 mm from the skin surface and by the posterior breast tissue extent (chest wall and pectoralis muscles not included) and other structures including *Air/Seroma*, *Heart*, *Normal Tissue*, *Chest Wall*, *Ipsilateral Lung* and *Skin Surface*.

When reconstructing the cavity, we always aim for replicating the physical dimensions of the SAVI applicator (Figure 7), according to the manufacturer's specifications.

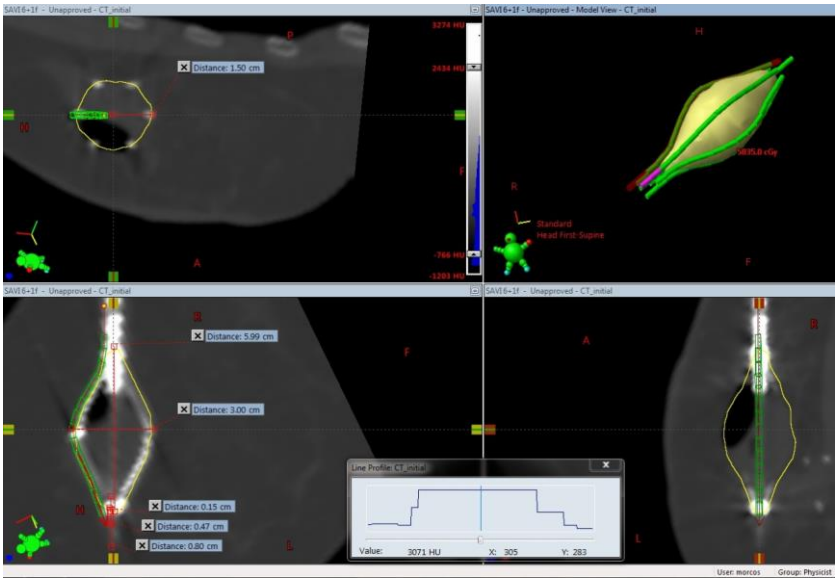


Figure 7. SAVI6+1 reconstructed cavity and applicators

The standard fractional dose is of 340 cGy to the outer surface of PTV_EVAL. The total dose of a full course of treatment is of 3400 cGy, delivered in 10 fractions, twice daily, with daily pair-fractions at least six hours apart. The planning criteria used for planning are matching the once recommended by the NSABP B-39/ RTOG 0413 protocol guidelines for APBI irradiation with respect to D90, V100, V150, V200 and conformity indexes, as well as to Maximum Skin Dose (MSD). V100, V150 and V200 represent the volumes (in cm^3) covered by the respective (IL) isodose line (in %).

As stated before, the main precursors of the SAVI device were two balloon-type devices, the later being the Contura™ MLB applicator, a five (5) lumen balloon-type device, clinically launched in January 2008 by SenoRX, Inc, believed to be a better solution for certain cases unfit for PBI (partial breast irradiation) using the similar original device, the MammoSite (Hologic) single-lumen balloon, due to either minimal balloon-to-skin distance, balloon symmetry or tissue-balloon conformance. In this section we present our dosimetrical evaluation of both balloon-type applicators against each other and relative to the SAVI device, in a comparative study (**Morcovescu** *et al*., 2009) meant to highlight the relevant advantages of one balloon type device over the other, and of the SAVI device over both balloon type devices, in view of the RTOG 0413 protocol.

We considered ten (10) cases elected to be treated with the Contura™ balloon. The treatment plans were designed following the RTOG 0413 planning guidelines. All five (5)

available channels were used when creating plans with the Contura™ balloon, as shown in Figure 8.

Figure 8. Contura™ balloon, all 5 channels fully loaded

Surrogate plans were then designed for each of the ten cases, using only the centered lumen of the Contura™ balloon, in order to mimic the use of a MammoSite-contura (MMc) applicator. For each patient, the outcome of the three plans were then compared and analyzed both from a dosimetrical perspective and from the treatment delivery hands-on experience perspective as well.

The SAVI device was the applicator of choice in our first two SAVI cases because of the small lumpectomy cavity sizes, 9.6cc and 8.5cc respectively. These two cases were evaluated in a comparison with the other two commonly used APBI treatment balloon-type devices, the MammoSite and the Contura balloons. A Contura plan template was also superimposed on the CT image set and fit into the cavity volume. A plan was then created as to deliver the prescription dose to the same PTV surface as the one considered for the MammoSite virtual plan.

When comparing the balloon type applicators, the intrinsic design of the Contura™ MLB applicator corroborated with an automated plan optimization process that considered the use of all its five (5) channels, contributed to a generally better dosimetrical characterization of the target volumes, when trying to limit the Maximum Skin Dose (MSD) to less than 145% of the Prescription Dose (PD). Coverage Indexes for both PTV and PTV_EVAL structures, as defined in the RTOG 0413 protocol, were evaluated. With Contura, the PTV Coverage Index – CI_1 is better by an additional 1.5–3.5% compared to

the MammoSite (MM) balloon. An increase of V150 and V200 values were recorded for Contura compared with MM, in the range of 1.0-2.0 cc (V150) and 0.1-1.0 cc (V200), while maintaining acceptable limits for both. The most common limiting factor for the use of interstitial PBI is the MSD. While improving the coverage of both PTV and PTV_EVAL with the Contura, the MSD was reduced by 8.0-12.0% of PD compared to the MM. Close and thorough monitoring of the balloon positioning during the treatment course is also essential, as rotation of the balloon may occur. Overall, compared to the simulated MammoSite-Contura balloon, better target coverage was possible with the new Contura^{TM} MLB applicator while being able to reduce the MSD values and to achieve better conformity.

When comparing the cases where the SAVI device was elected against the MM and Contura balloon devices, the following results are reported. Lumpectomy cavity volumes of less than 10 cm^3 were easily accommodated by the SAVI6-1mini. Because of possible differential loading of up to 7 catheters, even cases that would normally not meet the criteria outlined in NSABP B-39 can were successfully treated without any clinical and dosimetrical compromises. In general though, studies show that plans done with both balloon-type and SAVI devices conform well to guidelines specified in national protocols (Scanderbeg *et al*., 2009; Sehgal *et al*., 2011). The 95% isodose line coverage in all three situations is very similar, in the 96.5% – 99.8% range. Though, the maximum skin dose and the maximum rib dose vary greatly, especially for the case where the recorded SAVI-to-skin distance was 1.3 mm.

Table 2. Comparison data for Contura, MM and SAVImini cases

#	Applicator type	V100 (cc)	V95 (%)	V90 (%)	V150 (cc)	V200 (cc)	DHI	Max skin dose (%)	Max CW dose (%)	PTV volume (cc)	Min Skin Distance (mm)
1	miniSAVI	47.2	98.6	99.6	27.4	17.1	0.419	72.5	170.3	48.92	13.9
	MM1dw	73.3	96.5	98.3	25.1	5.1	0.658	147.2	355.7	82.0	
	Contura	77.0	99.1	99.8	28.7	7.8	0.627	143.0	325.3		
2	miniSAVI	24.8	97.0	98.7	16.0	10.2	0.355	105.7	163.9	26.3	1.3
	MM1dw	78.4	98.4	99.0	30.0	8.2	0.617	582.7	323.1	82.0	
	Contura	79.4	99.3	99.6	31.6	9.5	0.602	592.8	280.1		

Balloon-type applicators cannot accommodate volumes of less than 15cc without causing extreme patient discomfort, skin overstretching and prohibitive skin doses, up to almost 600% of the prescription dose, as our study shows. Maximum skin doses of 244.3% (MM) and 249.4 % (Contura) were estimated when the body surface was conformed to the shape of a balloon applicator (Table 2).

Because of the size of the cavity in the case of SAVI6-1minis, V150/V100 volume ratios tend to exceed the 0.5 value, therefore further investigation and reevaluation of the DHI acceptance criteria, and relevance, for APBI for small cavity volumes is necessary. Balloon-type applicators like MammoSite or Contura can accommodate a large range of clinical situations but fail to address the ones where the lumpectomy cavity volumes are below 15cc. The SAVI6-1mini applicator proves to be the only implant solution for those small lumpectomy volumes, below 15cc. Its design allows a proper dose optimization, with excellent PTV coverage and acceptable skin sparing. Our study indicate that the SAVI device proves to be a desirable option for small lumpectomy cavities and short skin bridges, with excellent coverage results and minimal skin reactions and late secondary effects.

CHAPTER 6 COMPREHENSIVE DOSIMETRIC ANALYSIS OF THE SAVI DEVICE

With the evolvement and development of different technologies designed specifically for the treatment of breast cancer alone, another important additional aspect that is crucial to the implementation of a comprehensive (APBI) accelerated partial breast irradiation program is a robust quality assurance program that confirms that the treatment target is appropriately defined and dosimetrically covered within the intended prescription dose (Wazer *et al*., 2006), and that the organs at risk are not irradiated above widely accepted and protocol imposed tolerance values (NSABP Protocol B-39/RTOG 0413 Protocol, 2007), when also confronted and confirmed with values obtained by the application of novel computational algorithms such as Acuros or Monte-Carlo (Graf *et al*., 2011).

Our preliminary studies (Morcovescu *et al*., 2009; Morcovescu & Morton, 2009) indicated that the SAVI device's dosimetric performance is superior to that of balloon type

APBI devices, so we further attempted to comprehensively evaluate the dosimetric performance of SAVI type devices.

The main body of our work consists on a comprehensive dosimetric analysis of extensive clinical data, collected for all four different size SAVI devices (SAVI6-1mini, SAVI6-1, SAVI8-1 and SAVI10-1). Our study is structured and focused on two subsets of data: 1) a major pool of data collected at a multi-institutional level, that presents the dosimetric analysis of the entire range of SAVI applicators, and a 2) minor pool, a subset of the entire data, considering patients implanted with the smallest of the SAVI devices, the SAVI6-1mini device, in our clinic only. The total number of patients included in our multi-institutional pool study is 817. There were 14 different participating institutions involved in the multi-institutional study, each providing data for all four SAVI device models. The subset study presented on the SAVImini device is a single-institution study of plans created for 121 patients, treated over the span of 5 years, from 2009 to 2014.

The dosimetric parameters reported in this study include: cavity volume, volume of the defined treatment region (PTV_EVAL), V90(%), V95(%), V100(%), V150(cc), V200(cc), skin distance (minimum distance from the lumpectomy cavity wall to the skin), chest wall and ipsilateral lung distances (mm), and the maximum doses to critical structures (skin and chest-wall). Conformity Indexes (CI), related to reported air/seroma and invagination volumes, were also evaluated, and shown in tables from Table 5 to Table 29. Our dosimetric coverage criteria for this study was V90>90%, V150<50 cm^3, V200<20 cm^3. Additional constraints are placed to try limiting the chest wall and skin doses to 100%. All dosimetric data, both the major pool and minor subset, was stratified using 5 mm skin-distance (SD) intervals, therefore differentiating among cases with major or no PTV volume reduction.

We have also evaluated and reported the volumes of the cavity, of the PTV and of the PTV_EVAL, and evaluated the volume reduction of the PTV. For this we proposed and used this equation for calculating PTV-VR:

$$\text{PTV-VR (\%)} = (\text{PTV volume} - \text{PTV\_EVAL volume}) / \text{PTV volume} \quad \textbf{(6.1)}$$

The Task Group TG43 formalism was employed on all dosimetric evaluations, and both TG43 and ACUROS formalisms used on the SAVI6-1mini device study only.

TG43	V90	V95	V100	V150	V200	V cav	V PTV	V PTVe	Max Skin D	Min Skin	Max CW D	Min CW
	%	%	%	cc	cc	cc	cc	cc	cGy	mm	cGy	mm
n =	762.0	637.0	768.0	665.0	758.0	514.0	532.0	693.0	687.0	470.0	419.0	317.0
MEAN	96.5	93.7	89.9	28.6	14.0	28.7	90.9	66.9	2884.3	12.1	2565.0	15.8
MEDIAN	97.5	94.8	90.9	26.7	13.8	24.6	78.8	62.0	2954.0	10.0	2620.0	13.0
MINIMUM	75.2	70.9	65.7	8.2	3.7	2.8	14.6	14.2	120.0	0.5	217.6	0.0
MAXIMUM	100.0	100.0	100.0	70.1	38.7	78.4	202.8	160.1	7854.0	76.4	6730.0	93.5
STANDARD DEV	3.2	4.5	5.7	9.1	4.1	18.0	39.5	24.7	942.8	9.5	1152.5	13.8

Table 3. Full data, for all SAVI devices (above)

Table 4. Sorted Data for the SAVI10-1 device (below)

TG43	V90	V95	V100	V150	V200	V cav	V PTV	V PTVe	Max Skin D	Min Skin	Max CW D	Min CW
	%	%	%	cc	cc	cc	cc	cc	cGy	mm	cGy	mm
n =	115.0	80.0	123.0	82.0	109.0	96.0	89.0	101.0	103.0	84.0	81.0	68.0
MEAN	97.0	94.6	90.7	41.7	17.5	57.6	148.3	105.5	2786.3	12.9	2538.0	15.8
MEDIAN	97.8	95.2	91.1	42.4	17.6	58.6	155.0	107.6	2850.0	10.4	2689.4	13.2
MINIMUM	90.3	82.8	75.6	19.2	6.3	29.4	49.7	49.7	500.0	1.0	250.0	1.0
MAXIMUM	100.0	100.0	99.3	70.1	36.5	78.3	202.8	160.1	6543.0	50.0	4284.0	93.5
STANDARD DEV	2.6	3.8	4.8	6.9	3.8	9.4	31.8	18.1	886.0	10.7	979.7	15.1

ACUROS	V90	V95	V100	V150	V200	V air/seroma	V invag	VR	Ipsi Lung d	Max Skin D	Max CW D
	%	%	%	cc	cc	cc	cc	cc	mm	cGy	cGy
n =	4	4	4	4	4	4	4	4	4	4	4
MEAN	99.68	98.93	97.18	26.70	15.33	6.40	0.00	0.00	20.53	1218.0	2508.5
MEDIAN	99.65	98.90	97.30	27.20	15.75	4.15	0.00	0.00	21.25	1117.0	2251.5
MINIMUM	99.50	98.50	96.00	23.80	13.30	1.30	0.00	0.00	11.40	918.0	1409.0
MAXIMUM	99.90	99.40	98.10	28.60	16.50	16.00	0.00	0.02	28.20	1720.0	4122.0
STANDARD DEV	0.17	0.40	0.87	2.23	1.47	6.89	0.00	0.01	6.92	357.8	1146.8

Table 5. SAVImini data, SD>25mm ACUROS (above)

Table 6. Stratified dosimetry for 5mm SD grouping interval (below)

Skin Distance	#	Max Skin Dose (Gy)		PTV reduction	CW Dose (Gy)	
mm	patients	TG43	Acuros	(%)	TG43	Acuros
< 5	13	35.94	**33.71**	37.0±12.0	32.9±19.5	**32.2±20.6**
5 < s.d. <10	20	33.25	**31.77**	17.0±8.0	35.2±15.3	**34.0±16.1**
10<s.d.<15	20	31.1	**30.6**	4.0±7.0	31.6±19.7	**31.0±20.7**
15<s.d.<20	8	26.66	**25.43**	6.0±16.0	28.0±16.0	**26.9±15.4**
20<s.d<25	7	18.87	**18**	0.0±1.0	32.3±13.5	**31.4±13.4**
s.d > 25	4	18.16	**17.2**	0.0±1.0	25.1±11.5	**24.4**±8.8

Skin Distance		Max Skin Dose (Gy)		PTV_EVAL			Normal Tissue		PTV reduction† (%)	CW Dose (Gy)	
mm	# patients	TG43	Acuros	V90(%)	V95(%)	V100(%)	V150(cc)	V200(cc)		TG43	Acuros
< 5	**13**	35.94	**33.71**	**95.3±2.8**	**92.9±3.5**	**90.0±4.1**	17.5±3.8	10.0±1.8	37.0±12.0	32.9±19.5	**32.2±20.6**
5 <SB<10	**20**	33.25	**31.77**	**97.6±1.2**	**95.9±1.4**	**93.3±1.9**	23.6±2.9	13.7±2.0	17.0±8.0	35.2±15.3	**34.0±16.1**
10<SB<15	**20**	31.1	**30.6**	**98.8±1.8**	**97.6±2.5**	**95.3±3.2**	27.0±3.0	15.9±2.2	4.0±7.0	31.6±19.7	**31.0±20.7**
15<SB<20	**8**	26.66	**25.43**	**99.8±0.2**	**98.8±0.8**	**96.6±1.8**	27.8±1.5	15.5±1.3	6.0±16.0	28.0±16.0	**26.9±15.4**
20<SB<25	**7**	18.87	**18**	**98.9±1.9**	**97.8±3.7**	**95.7±6.0**	27.0±4.3	15.2±2.9	0.0±1.0	32.3±13.5	**31.4±13.4**
SB>25	**4**	18.16	**17.2**	**99.7±0.2**	**98.9±0.4**	**97.2±0.9**	27.3±2.4	15.6±1.6	0.0±1.0	25.1±11.5	**24.4**±8.8

Table 7. SAVImini centralized data (TG43 and ACUROS)

Tables 3 through Table 7 are sample tables presenting the data for both the multi-institutional and single-institution studies. The bulk data was stratified based on the distance from the device to the skin, in increments of 5mm. Our dosimetric coverage criteria for this study was V90>90%, V150<50 cm^3, V200<20 cm^3. Additional constraints are placed to try limiting the chest wall and skin doses to 100%. All dosimetric data was stratified using 5 mm skin-bridge intervals, therefore differentiating among cases with major or no PTV volume reduction.

For the multi-institutional study on all SAVI type devices the following results are reported:

1) The lumpectomy cavity volumes averaged 10.5±3.3 cm^3 for the 6-1SAVImini device up to 57.6.5±9.4 cm^3 for the largest 10-1 SAVI applicator.
2) PTV_EVAL volumes averaged 45.1±9.3 cm^3 for the smallest applicator to 105.5±18.1 cm^3 for the largest. V90 values averaged 96.5±13.2% of the PTV_EVAL volume across all applicator sizes, which is well within the criteria imposed by the NSABP B-39/RTOG 0413 protocol. V95 averaged 93.7±4.5% and V100 averaged 89.9±5.7%. V150 averaged 23.2±5.7 cm^3 for the smallest device, and 41.7±6.9 cm^3 for the largest. V200 averages ranged from 12.5±3.0 cm^3 for the smallest device, to 17.5±3.8 cm^3 for the largest.
3) The Mean, Median, Maximum, Minimum and SD values for V90, V95, V100, V150 and V200 of PTV_EVAL are reported in Table 8. Similar data for Cavity, PTV, and PTV_Eval Volumes is reported in Table 9.
4) Skin spacing varied widely with 460 reported values ranging from 0.5 mm to 76.4 mm (12.1 ± 9.5mm). Skin spacing in these patients were: ≤3 mm (9.4%), 3-5 mm (13.2%), 5-7 mm (10.9%), >7 mm (66.6%). The minimum skin bridge for these patients averaged 12.1 mm, although each model was used in patients with ≤3.0 mm (44, total).
5) The maximum skin dose (n=687) was 85%±28% of prescription (mean ± SD). From smallest to largest models, the values were: 82%±26%, 84%±24%, 87%±29%, 84%±28%.
6) Chestwall bridge varied widely (n=317), ranging from 0.0 mm to 93.5 mm (15.8 ± 13.8mm), and was similar regardless of model. For each applicator size, the maximum dose to the chest wall was 75% ± 34% of the prescription dose.

Table 8. Multi-institutional, all SAVI type devices - values for V90, V95, V100, V150 and V200 of PTV_EVAL

Parameter	V90	V95	V100	V150	V200
(units)	%	%	%	cc	cc
MEAN	96.5	93.7	89.9	28.6	14.0
MEDIAN	97.5	94.8	90.9	26.7	13.8
MINIMUM	75.2	70.9	65.7	8.2	3.7
MAXIMUM	100.0	100.0	100.0	70.1	38.7
SD	3.2	4.5	5.7	9.1	4.1

Table 9. Multi-institutional, all SAVI type devices - values for Cavity, PTV, and PTV_Eval Volumes

Parameter	V(cavity)	V(PTV)	V(PTV_Eval)
(units)	cc	cc	cc
MEAN	28.7	90.9	66.9
MEDIAN	24.6	78.8	62.0
MINIMUM	2.8	14.6	14.2
MAXIMUM	78.4	202.8	160.1

For the single-institutional study on all SAVI6-1mini type device for which TG43 computational algorithm was used, the following results are reported:

1) The lumpectomy cavity volumes for the SAVI6-1mini device, the device of interest for our initial study on this SAVI device subtype (**Morcovescu** *et. al*, 2009), averaged 8.3±0.9 cm^3.
2) PTV_EVAL and PTV volumes averaged 43.2±9.0 cm^3 and 49.5±3.8 cm^3, respectively. V90 values averaged 98.5±1.9% of the PTV_EVAL volume, which is again well within the criteria imposed by the NSABP B-39/RTOG 0413 protocol. V95 averaged 97.4±2.8% and V100 averaged 95.3±3.4%. V150 averaged 24.4±4.7 cm^3 while V200 averaged 14.1±2.9 cm^3.
3) PTV reduction mounted up to 37.0±12.0% for the cases where the skin distance (SD) was < 5 mm, especially where combined with reduced Chest Wall bridges (CWB). This can result in dramatic drops of the CI (conformity

index) values for PTV_EVAL, where air/seroma is present, down to 61.1%. Though, across the entire cohort, CI values averaged 96.6±5.7 %.

4) Skin and CW sculpting of PTV is always employed when creating PTV_EVAL structures. The PTV volume reduction PTV_{VR} averaged 13.0±16.0%, with min and max values of 0.0% (no reduction) and 59.0% (when both SB and CWB were < 5mm) respectively.
5) Thirteen (13) patients had a skin bridge (SD) of less than 5 mm. For these patients, the V90 (n=13) was 96.1±2.8% (mean±standard deviation). Chest wall bridge (CWB) varied widely, ranging from 0.3 mm to 61.0 mm (15.2±11.7 mm).The maximum dose to the chest wall, over the entire cohort of patients, was 94.5±49.5% of the prescription dose. Dosimetric data for a later study of ours (**Morcovescu** *et al*., 2014), which included 121 patients, is shown in Table 10. No major variation from the numbers previously published is observed.
6) The maximum skin dose for the patients where the skin distance SD was less than 5 mm was 96.0±4.9%. Chest Wall bridge varied widely, ranging from 0.3 mm to 61.0 mm (15.7 ± 12.0mm). The maximum dose to the chest wall, over the entire cohort of patients, was 94.5% ± 49.5%.
7) The V150 "hotspots" averaged 24.4±4.7 cm^3, while V200 averaged 14.1±2.9 cm^3. The average minimum skin distance was 13.5 mm, but the applicator was used in patients where the skin bridge was as low as 1mm. The average maximum skin dose (MSD) was 72.8% of the prescription dose. The average minimum CWB was 15.2 mm, with the shortest of less than 0.3mm, and the average maximum dose to the chest wall of 90.5% of the prescription dose.

Table 10. Stratified dosimetry for 5mm skin-distance grouping interval

Skin Bridge (mm)	# Patients	Max Skin Dose (Gy)	V90 (%)	V200 (cm^3)	PTV_{VR} (%)
< 5	16	35.94	96.3±2.3	10.1±1.7	36.0±12.0
5 <SB <10	34	33.25	98.4±1.2	13.4±1.7	16.0±7.0
10 <SB <15	31	31.78	99.3±1.2	16.0±1.9	3.0±6.0
15 <SB <20	14	26.66	99.9±0.2	15.7±2.2	4.0±12.0
20 <SB <25	16	18.87	99.6±2.5	15.6±2.1	1.0±3.0
SB > 25	10	18.16	99.6±0.4	16.4±2.3	0.0±1.0

8) The PTV-VR values are largest for the cases with reduced skin bridges, where there is a significant reduction of the volume of PTV_EVAL compared to PTV. Dose coverage in those marginal cases was still excellent, with average V90 of 96.3%.

The Mean, Median, Maximum, Minimum and SD values for V90, V95, V100, V150 and V200 of PTV_EVAL are reported in Table 11. Similar data for Cavity, PTV, and PTV_Eval Volumes is reported in Table 12.

Table 11. Single-institution, SAVI6-1mini type device - values for V90, V95, V100, V150 and V200 of PTV_EVAL

Parameter	V90	V95	V100	V150	V200
(units)	%	%	%	cc	cc
MEAN	98.0	96.5	94.1	24.4	14.1
MEDIAN	98.9	97.1	94.6	25.9	14.7
MINIMUM	89.9	86.3	82.2	10.9	6.5
MAXIMUM	100.0	100.0	99.7	31.3	20.0
SD	2.3	3.1	3.9	4.7	2.9

Table 12. Single-institution, SAVImini type device - values for Cavity, PTV, and PTV_Eval Volumes

Parameter	V(cavity)	V(PTV)	V(PTV_Eval)
(units)	cc	cc	cc
MEAN	8.3	49.5	43.2
MEDIAN	8.3	49.6	47.1
MINIMUM	6.2	25.7	14.2
MAXIMUM	10.4	57.9	53.9
SD	0.9	3.8	9.0

The PTV to PTV_EVAL volume reduction may be large for SB < 5mm (37.0±12.0), but plans still met all other dosimetric criteria. Less PTV reduction, 17.0±8.0 (5mm<s.d.<10mm), and 4.0±7.0 (10mm<s.d<15mm) results in better dose conformity/critical structure sparing.

For the single-institutional study on all SAVI6-1mini type device for which the Acuros computational algorithm was used, the following results (Morcovescu *et. al*., 2012) are reported:

1) V90 values averaged 98.0±2.3% of the PTV_EVAL volume, V95 averaged 96.5 ±3.1% and V100 averaged 94.1±3.9%. V150 averaged 23.9±5.4 cm^3 while V200 averaged 13.8±2.8 cm^3. The values indicate a small but quantifiable degradation of the PTV_EVAL coverage compared with when employing the TG43 protocol for calculations.
2) The maximum skin dose for the patients where the skin distance SD was less than 5 mm was 91.7±5.2%.
3) The maximum dose to the chest wall, over the entire cohort of patients, was 92.0% ±51.3% of the prescription dose.

Stratified dosimetry for all 72 patients is centralized in Table 13.

Table 13. Stratified dosimetry for 5mm skin-distance grouping interval

Skin Bridge (mm)	# Patients	Max Skin Dose (Gy)	V90 (%)	V200 (cm^3)	Max CW Dose (Gy)
< 5	13	33.71	95.3±2.8	9.9±2.0	32.2±20.6
5 <SB <10	20	31.77	97.6±1.2	13.2±2.0	34.0±16.1
10 <SB <15	20	30.6	98.8±1.8	15.4±2.0	31.0±20.7
15 <SB <20	8	25.43	99.8±0.2	15.5±1.3	26.9±15.4
20 <SB <25	7	18	98.9±2.5	14.9±2.7	31.4±13.4
SB > 25	4	17.2	99.7±0.2	15.3±1.5	24.4±8.8

All data reported and pertaining to both the multi and single institution studies clearly show that all SAVI devices allow for excellent PTV_EVAL coverage, in all encountered clinical situations. This is achieved while concomitantly being able to keep the skin and chest wall maximum doses below protocol imposed values (NSABP Protocol B-39/RTOG 0413 Protocol, 2007). Because of its versatility in dose shaping and adaptable device design, the SAVI6-1mini was successfully used in the treatment of a stenotic distal vagina as well (**Morcovescu** *et al*., 2016).

Our study on the smallest SAVI6-1mini device indicate that it can efficiently be used in clinical situations where stringent limitations are imposed by close proximity of the lumpectomy cavity either to the skin or chest wall. Even for situations where SB < 5 mm all PTV coverage criteria are met, while avoiding skin overexposure.

Another dosimetry study of ours on 108 all-type SAVI devices (Reiff *et al*., 2013) used on patients where the distance from the applicator to both skin and ribs were less than 7 mm indicates that the doses on all critical structures were within tolerable limits, as recommended by standard protocols or society accepted standards (Smith *et al*. 2009).

The SAVI6-1mini strut-based device is an excellent APBI solution for patients with reduced skin and/or rib bridges, and it accommodated volumes unfeasible for other types of single-entry brachytherapy devices. The Acuros data indicates a minor degradation of the RTOG 0413 reference V90 coverage of the PTV_EVAL (0.5% on average) while revealing that TG43 slightly overestimates the average dose values for skin (by 4.1%) and for chest-wall (by 2.6%). These results are confirmed by more recent studies on the impact of heterogeneity correction implications on brachytherapy planning, all indicating minimal effects on the average values of PTV coverage and maximum dose usually in the range of 2%, and 4% respectively (Loupot *et al*., 2014; Slessinger *et al*., 2012), but sometimes as high as 5%, and 7% or 10% respectively (Zhang et al., 2012; Likhacheva *et al*., 2016; Thrower et al., 2016), with variations due to placement of the device or heterogeneity information.

CHAPTER 7 COMPREHENSIVE EVALUATION OF A STRUT-ADJUSTED-VOLUME-IMPLANT SAVI DEVICE QUALITY ASSURANCE PROGRAM

Considering the complexity of the entire treatment process involving APBI cases and other brachytherapy procedures in general, there is a need of designing a comprehensive quality assurance program, as already done for other specific brachytherapy procedures (Brown *et al*. 2016) but also specifically for APBI (Cui *et al*., 2011; Chilukuri, 2016), that deals with all stages of this process taking place in a radiotherapy department: 1) the QA of the cavity and device localization and reconstruction, 2) the QA of the treatment plan, 3) the QA at the time of treatment and 4) the post treatment QA. We discuss all those in sequence and we highlight the common practices and the extra measures we included into our customized QA program, in an attempt to incorporate our clinical experience with the device into a comprehensive QA program capable of preventing and addressing even the least frequent clinical situations. A number of recent retrospective studies (Iftimia *et al*., 2015; Shah *et al*., 2016; Pinn-Bingham et al., 2011) clearly outline a variety of clinical factors and situations that can have a major impact on the outcome of high-dose-rate brachytherapy treatments, encompassing all stages of a QA program, from pre-delivery to

post-delivery, and emphasizing its importance in the cases of any type of breast brachytherapy type applicators (Kyriacou, 2016; Pinder *et al*., 2016).

The implementation of a comprehensive quality assurance of a brachytherapy program is mandatory by state and federal regulations (Kutcher *et al*.,1995), and its effectiveness and thoroughness vital for a successful delivery of brachytherapy treatments (Wazer *et al*., 2006). A number of studies on partial breast irradiation applicators clearly indicate the variety of clinical situations raising concerns and requiring special attention such as: impact of breast augmentation (Akhtari *et al*., 2015; Bloom *et al*., 2011), inter-fractional displacement or motion of SAVI devices (Chandrasekara *et al*., 2015; **Morcovescu** *et al*., 2011; Park et al., 2011; Hyvarinen *et al*., 2014), presence of air/fluid single or cluster cavities (Harmon *et al*., 2013. All these studies are clearly indicative of the impact all these possible factors can have on the final outcome of these types of treatments, and emphasizes the importance of having a carefully designed QA program.

The imaging sequence is an important part of the planning process. In our clinic, a patient is usually scheduled for a CT planning simulation and a CT is acquired the day following the implant surgery, in order to allow time for adequate tissue conformance around the SAVI device (Liu *et al*., 2012). During the initial planning scan done using a GE Lightspeed, large-bore, 4 slice CT scanner (GE Medical Systems, Waukesha, Wisconsin), two CT scouts, one anterior and one lateral, are acquired. For a high quality image reconstruction, we use 2.5 mm slice thickness for CT planning scan, extending at least 5 cm superiorly and inferiorly to the SAVI defined cavity area, typically resulting in a number of transverse images of around 65 slices. We employ a breath-hold during the CT scan, or at least we instruct the patients having breathing difficulties to exert a shallow breath pattern during the actual scan, in order to minimize respiratory motion artifacts.

M2, M4 and M6 markers are identified with the built-in markers of the SAVI devices, pertaining to their corresponding catheter number, 2, 4 or 6. We evaluate distances between the three pairs of strut markers in the AP or Lateral CT scouts, Figure 9, and compare, record and review these values prior to each fractional treatment.

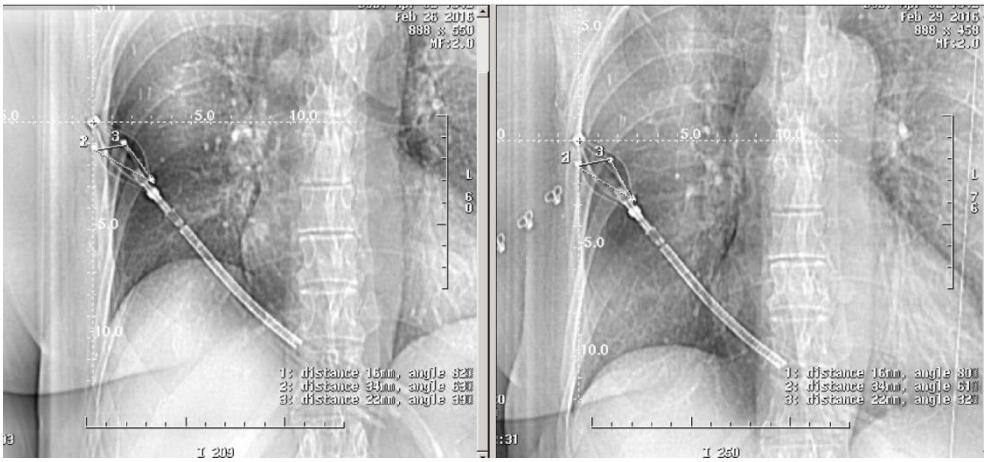


Figure 9. Pre-fractional comparison and review of implant placement: daily CT scout (right image) compared against original planning CT scout (left image)

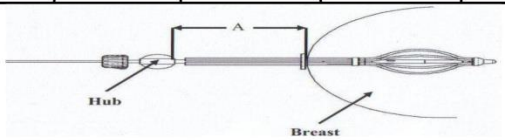
An in-house form, Figure 10, was developed in order to document and record relevant position parameters for the initial planning scan and for all subsequent pre-treatment verification scans. Several items need to be recorded on this form, which we generically refer to as the "SAVI daily CT checks and measurements" sheet.

Radiation ONCOLOGY Department

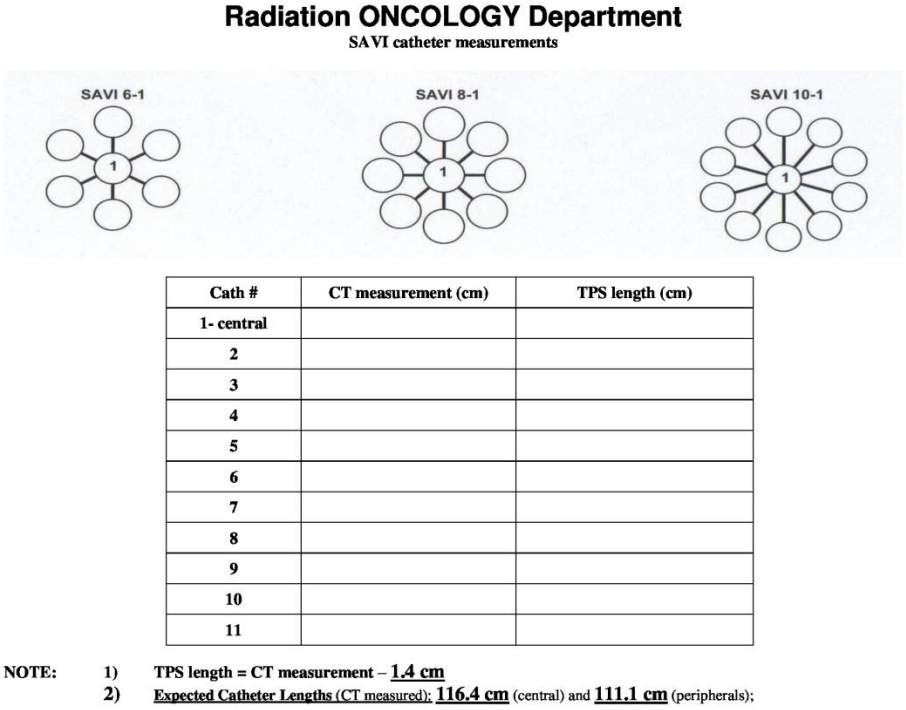
SAVI DAILY CT CHECKS AND MEASUREMENTS

Patient Name:_____; **Patient ID:**_____; **Left / Right BREAST;**

SAVI applicator type: _____; **Catheter Exits: Medial / Lateral;** **# of CT slices above / below SAVI:**_____

MEASUREMENTS	PLAN	DAY 1		DAY 2		DAY 3		DAY 4		DAY 5	
		Fx. 01	Fx. 02	Fx. 03	Fx. 04	Fx. 05	Fx. 06	Fx. 07	Fx. 08	Fx. 09	Fx. 10
Long axis length (mm)											
M2 – M4 Marker Distance (mm)											
M2 – M6 Marker Distance (mm)											
Max Expansion (mm)											
Min. SAVI – chest wall distance (mm)											
Min. SAVI – skin distance (mm)											
CT TECH											
PHYSICIAN											
DATE											
Catheter Measurements									Position of skin-cath **marker**		
NOTES											

NOTE: Measurements will be performed for each CT set of images related and taken prior to individual SAVI HDR treatment fractions. It is recommended that the same person - the CT Tech - perform all the measurements. The PHYSICIAN will check and approve the usage of each individual set of CT images.



Radiation ONCOLOGY Department

SAVI catheter measurements

SAVI 6-1 SAVI 8-1 SAVI 10-1

Cath #	CT measurement (cm)	TPS length (cm)
1- central		
2		
3		
4		
5		
6		
7		
8		
9		
10		
11		

NOTE: 1) **TPS length = CT measurement – 1.4 cm**

2) **Expected Catheter Lengths** (CT measured): **116.4 cm** (central) and **111.1 cm** (peripherals);

Figure 10. Front page (above) and Verso page (below) of our QA form

One major purpose of our work was to generate a tabular nomogram of treatment times for strut-based APBI applicators, intended to provide guidance and a pre-treatment quality assurance check for clinics establishing new treatment techniques or transitioning from balloon-based applicators.

A retrospective analysis was conducted of 486 patients receiving APBI using the SAVI strut-based applicators at three separate institutions. Patient data was organized based on applicator size (a surrogate of treatment volume) and number of organs at risk.

Three organs at risk categories were determined based on the proximity of the device to the patient's skin and/or chest wall (0, 1, or 2 OARs). Organs at risk were defined as being < 5 mm from cavity wall/peripheral struts. A tabular nomogram of treatment time (based on a nominal 10 Ci source strength) was generated from descriptive statistics of each combination of applicator size and organs at risk category.

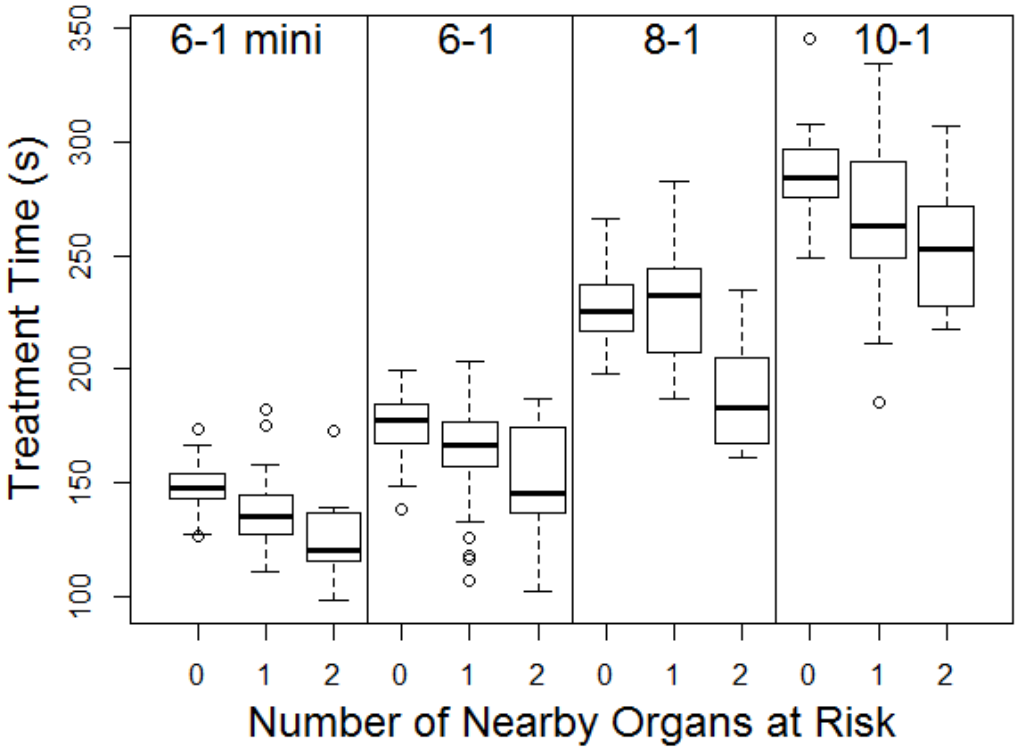


Figure 11: Boxplot of treatment times of various combinations of applicator size and Number of nearby organs at risk.

The treatment time was observed to be directly proportional to applicator size and, to a lesser extent, inversely proportional to the number of nearby organs at risk. Distributions of treatment times observed for each combination of applicator size and organs at risk category are depicted in Figure 11. The tabular nomogram featuring average treatment times with standard deviations is presented in Table 14.

Table 14: Tabular nomogram of average treatment times in seconds. Standard deviations are presented in parentheticals.

		Number of Nearby Organs at Risk		
		0	1	2
SAVI Applicator Size	6-1 mini	148.0 (9.4)	137.0 (14.4)	126.6 (19.1)
	6-1	175.7 (13.9)	165.7 (19.9)	152.1 (24.5)
	8-1	226.4 (16.0)	229.0 (25.0)	189.5 (25.0)
	10-1	287.2 (24.1)	269.4 (30.0)	252.6 (25.9)

Strut-based APBI treatment times were observed to depend in a consistent manner on applicator size and number of nearby organs at risk. Information provided in the nomogram presented here represents several hundred treatments performed at multiple institutions. This data can serve as guidance or quality assurance for institutions with limited experience using strut-based APBI applicators. This work distills considerable multi-institutional experience with strut-based APBI applicators into an accurate and pragmatic clinical tool that promotes treatment consistency and quality.

We also evaluated the effect on target coverage and organ of risk sparing caused by interfraction variance of a SAVI6-1mini APBI applicator (**Morcovescu** *et al*., 2011), in patients with small breast tissue volumes and limited skin/chest wall spacing. Daily setup combined with tissue conformance variations are confirmed to potentially have a big impact on dosimetric parameters in SAVI-based breast brachytherapy, as a number of recent studies indicate (Liu *et al*., 2012; Chandrasekara *et al*., 2015), therefore the outmost importance of a thorough QA of the planning process (Pella, 2016). Mammographic evaluation of an breast implant is also referred to as post treatment evaluation of an APBI treatment or plan (Ojeda-Fourier et al., 2011), but in this study we refer to the actual on-going dosimetric evaluation of a plan on subsequent CT data acquired during the treatment course itself.

Our study considered three (3) patients treated with a SAVI6-1mini device in our clinic. Individual Initial treatment plans were generated based on the original CT-SIM scans and saved as template plans for fractional re-planning. Pertinent dosimetrical parameters were evaluated and recorded (i.e., V200, V150, V100, V95 and V90, maximum skin and chest wall dose). The template plan was then superimposed on the subsequent pre-treatment fractional CT-Sim and tomography-based treatment plans were generated for Fractions 1-10. All pertinent structures were reconstructed as to closely fit the volumetric profiles of the initial plan structures. Relevant dosimetric comparison was then performed using the maximum doses to organs at risks, %PTV_EVAL and % PTV coverage, and target dose homogeneity index.

A total of 11 plans were generated for each patient, a total of 33 plans for the entire current study. Accurate reconstruction of the SAVI planning structure was an initial study objective, thus only variations of +/- 0.2 cc from the reference SAVI device volume in the initial CT-Sim scan were accepted. Minor PTV_EVAL volume changes of +/- 1.5 cc were

then estimated. The SAVI6-1mini applicator average rotational axial shift, over the course of the entire treatment, was $2.8^{o} \pm 2.1^{o}$, hardly assessable or detectable based on prefractional CT-sim and external skin marker positional checks.

We found that due to interfraction variance in local anatomy (i.e., altered SAVI to chest wall and skin distances, slightly changed skin surface contours, air/seroma profile difference), skin and chest wall dose escalations of up to 30% and PTV_EVAL V90 and V95 coverage degradation for and of up to 5% of the reported values on the initial plan can be observed.

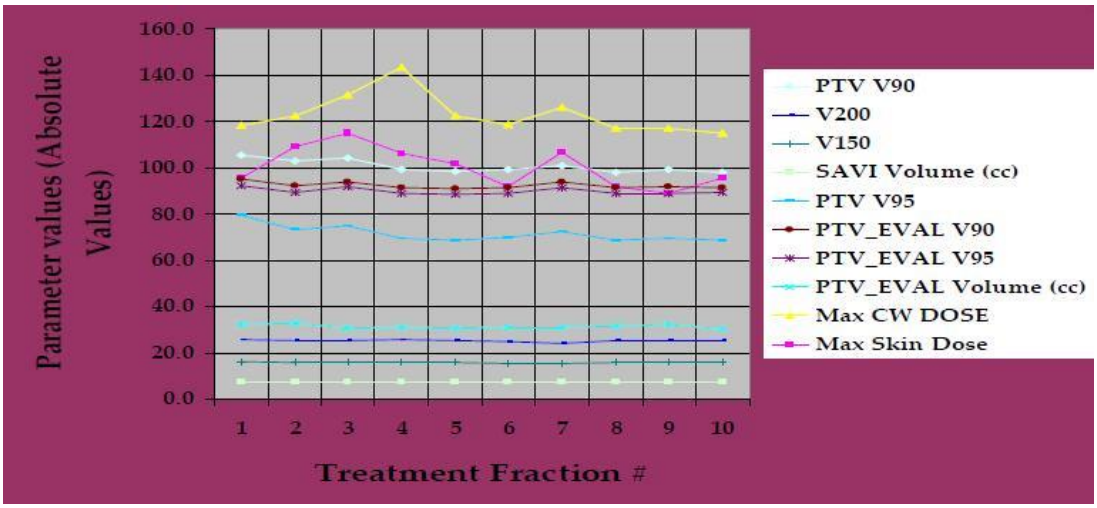


Figure 12. Absolute value inter-fractional variations of planning parameters

Variations on monitored parameters were recorded and trended, Figure 12. The highly sensitive parameters to rotational variances are the Maximum Doses to Skin and Chest Wall, which can mount to escalations of those values of up to 140% of the prescription dose.

The treatment time reduction, due to imposed to necessary cooling off of the dose on the skin or chest wall, and preservation of planning objectives, was up to 4.8% of the initial treatment time, when re-planning was employed. A summary of the data analysis for Patient 1 is shown in Table 15 below.

Table 15. Summary of the data analysis for Patient 1

Parameter	Average	SD	MAX	MIN
Max Skin DOSE (cGy)	100.2	8.34	115	89
Max CW DOSE (cGy)	123.2	8.19	144	115

PTV_EVAL Volume (cc)	31.3	0.77	32.7	30.2
PTV_EVAL V95(%)	89.8	1.35	92.3	88.3
PTV_EVAL V90(%)	92.3	1.31	94.9	91.0
PTV_EVAL V150cc)	15.7	0.24	16.2	15.2
PTV_EVAL V200(cc)	9.4	0.22	9.8	8.9
PTV V95(%)	71.5	3.32	79.4	68.6
PTV V90(%)	75.4	2.51	79.7	72.7
SAVI Volume (cc)	7.5	0.06	7.6	7.4

Individual differential source dwelling times adjustments, building up to as low as 3% of the total treatment time of the Initial plan, were sufficient for recovering the desired standard APBI planning objectives.

Routine pre-treatment CT scan checks are unlikely to point out hard-to-quantify local anatomy inter-fraction variances, therefore, carefully conducted pre-treatment QA procedures are mandatory for the correct delivery of a SAVI6-1mini APBI treatment and for the achievement of a high degree of conformance between the initial reference TPS plan and the clinically delivered plan (Morcovescu *et al*., 2016). Inter-fractional TPS plan re-evaluations should become a routine when dealing with cases where the applicator is very proximal to organs of risk and where highly asymmetrical PTV_EVAL volumes are employed, in order to avoid overlooking prohibitive sensitive structure doses and unacceptable treatment volume coverages.

The SAVI6-1mini strut-based device proves to be a highly adaptable APBI solution for patients with reduced breast and lumpectomy cavity volumes, and skin and/or chest wall bridges. Inside the framework of a detailed and clear QA program, when it is appropriately elected as the APBI device of choice, optimally implanted, and comprehensively monitored during the course of treatment, all SAVI device types, but the SAVI6-1mini in particular, indeed offer a very effective and highly reproducible tool for the treatment of complex breast cancer cases. Our analysis demonstrates the dosimetric versatility and outlines the clinical implementation process of the SAVI brachytherapy device, especially for APBI cases that require more flexible dose optimization, for both coverage of PTV volumes and sparing of dose to adjacent critical structures.

CHAPTER 8 CLINICAL RESULTS

The accelerated partial breast irradiation (or APBI) treatment technique has been widely embraced as an acceptable modality for delivering adjuvant radiation therapy for a selected group of patients undergoing breast-conserving therapy. The recently published GEC-ESTRO trial, a Phase III randomized prospective trial, and other recent studies (Polgar *et al*., 2004; Bitter *et al*., 2016) demonstrated superior cosmesis and noninferiority of APBI with brachytherapy when compared to whole breast irradiation (WBI). In this chapter we indicate the results of our own 5 year retrospective study on all SAVI device types (Yashar *et al*., 2016), reporting them in terms of local control, toxicity, and survival for the first 250 patients treated across multiple institutions.

Toxicity was graded according to the Common Terminology Criteria for Adverse Events version 3.0, commonly used in prospective toxicity analysis for breast cancer studies (Rehman *et al*., 2016), except seroma and fat necrosis, which were modified by the consortium to more appropriately fit APBI.

The median age of the 250 patients in this study was 62 years (range, 40-85), out of who 73.5% had invasive disease and the remaining 26.5% had pure ductal carcinoma *in situ*.). The majority (57%) of these women were older than 60 years, although 36 (14.4%) were younger than 50 years (11% were <45 years). Most patients were postmenopausal (84%), had estrogen receptor positive tumors (90%), received endocrine therapy (65%), and did not receive chemotherapy (91%).

For the 250 patients, the mean V_{90} was 96.1 ± 3.7%, V_{95} was 93.5 ± 6.1%, V_{100} was 90.4 ± 5.5 cc, V_{150} was 30.5 ± 11.0 cc, and V_{200} was 14.7 ± 5.1 cc. These dosimetric variables differed by device. Skin dose mean was 269 cGy (79.1% of prescription dose). For those patients with a skin bridge >3 mm and ≤5 mm or ≤3 mm, the mean values were 274 cGy and 281 cGy (80.7 and 82.7% of the prescription dose), respectively. The mean rib dose was 273 cGy (80.4% of the prescription dose).

In this cohort, all four sizes of applicator were used: 10-1 (21%), 8-1 (32%), 6-1 (38%), and 9% received the SAVI6-1mini size. More than half the patients had skin spacing less than or equal to 10 mm (44% > 10 mm) with 12% and 17% having skin bridges of 3-5 mm and ≤3 mm, respectively. Of the entire population, 85.9% had

excellent/good cosmesis at 60 months. Ten of the 11 reporting sites had excellent/good cosmesis in 96.2%, and in one center, excellent/good cosmesis was reported in 57.9%.

Dosimetric targets were met in virtually all patients and are similar to other published series with excellent target coverage and normal tissue avoidance. With the struts adjacent to the target tissue, the allowable target for V_{200} is more similar to the interstitial target than the balloon target. But, as demonstrated in this series, this has not led to increased toxicity. A recent single institutional series compared a large cohort of patients (n=594) with APBI using different single-entry devices. This report also observed outstanding target coverage with excellent skin and rib sparing (Rana *et. al*, 2015). Associations between dose and telangiectasia were made possible based on univariate analysis. Since dose and skin spacing are related, and other publications have demonstrated a similar correlation, this is was of no surprise. Other possible correlations are made between V_{90} and V_{150} and symptomatic seroma, and V_{90} and fat necrosis, but the numbers were overall too small to trigger for a prompt alteration of guidelines.

The strengths of this report include its multi-institutional participation and robust numbers (n = 250) with the longest follow-up for a single-entry multilumen breast brachytherapy device. The selection criteria were practically unbiased, free of any screening filters, since it basically included the first 250 subjects accrued. It is limited by its retrospective nature, which may confound data as institutional toxicity reporting and treatment policies may differ.

CONCLUSIONS

Based on the results of our studies, we can conclude that the use of multilumen applicators clearly simplifies brachytherapy APBI compared to interstitial brachytherapy, allowing the advantages of brachytherapy over other forms of accelerated partial breast radiation therapy accessible to more women.

The clinical implementation of the SAVI device poses various challenges to the potential users, but within the frame of a robustly designed and implemented quality assurance program, all standard dosimetrical goals are achieved, including conformance to the tumor bed coverage and dose minimization to surrounding normal tissues, as indicated by other similar studies (Scanderbeg *et al*., 2009; Yashar *et al*., 2008).

We argue that the PTV_EVAL and PTV coverage goals achievable with the SAVI device, with mean V95 over 95% and mean V90% over 97%, way above the protocol required criteria of 90%/90%, on almost all possible clinical situations, is an assurance that the use of this APBI device can adequately compensate for random and systematic errors inherent in these type of treatments (Stojadinovic *et al*., 2008).

Even though the NSABP B-39/RTOG 0413 protocol imposes VHI criteria of 0.750 across all brachytherapy type applicators, therefore promoting rather restrictive criteria widely accepted and used for multi-catheter interstitial implant (Wu *et al*., 1988), our study indicates that the use of these same criteria is unfit for SAVI type devices. Our recommendation is that this parameter should not be used for the evaluation of the adequacy of plans in breast brachytherapy, when SAVI type devices are used, and if used, to relax the threshold value from 0.750 to a more realistic value of 0.500.

The use of the ACUROS formalism, when dose inhomogeneity corrections are applied in such a complex anatomical environment, where the presence of air pockets, seroma, breast tissue of different densities, proximity of the skin surface or of the rib cage can change the scatter and back scatter conditions dramatically, falls in line with theoretical predictions, showing that overall coverages and reported maximum doses to critical organs degrade slightly compared with those reported for when the standard TG43 algorithm is employed, more for skin average maximum reported doses (~ 4%) than for correspondent chest wall doses (~ 2%). These results are confirmed by more recent studies on the impact of heterogeneity correction implications on brachytherapy planning, all indicating minimal effects on the average values of PTV coverage and maximum dose usually in the range of 2%, and 4% respectively (Loupot *et al*., 2014; Slessinger *et al*., 2012), but sometimes as high as 5%, and 7% or 10% respectively (Zhang et al., 2012; Likhacheva *et al*., 2016; Thrower et al., 2016), with variations due to placement of the device or heterogeneity information.

The strut open architecture design and multiple catheter options allow dose sculpting to each patient's unique anatomy and cavity location. This flexibility helps to overcome prior concerns with skin spacing and tumor beds positioned between the overlying skin and chestwall that limited patient eligibility. The dosimetric parameters considered relevant for our studies, and data reporting of those parameters, namely especially Max Skin Dose, is accurately reflected in our clinical data outcome reports,

which indicates that the definitions in use for these parameters needed no reconsideration, as some studies suggest (Park *et. al*, 2016). The clinical report we contributed to with patient data confirms excellent tumor control comparable to other published APBI rates and survival with low toxicity, based on median 59.5 month outcomes for patients treated with the strut-based applicator. Compared to external beam techniques for APBI, SAVI brachytherapy seems to be as effective, with less toxicity.

THE LIST OF PAPERS PUBLISHED DURING THE DOCTORAL PROGRAM

Scientific Papers published in ISI impact journals

1. Yashar C., Attai D., Butler E., Einck J., Finkelstein S., Han B., Hong R., Komarnicky L., Lyden M., Mantz C., **Morcovescu S**., Nigh S., Perry K., Pollock J., Reiff J., Scanderbeg D., Snyder M., Kuske R., **2016**, *Strut-based accelerated partial breast irradiation: Report of treatment results for 250 consecutive patients at 5 years from multicenter retrospective study*, Brachytherapy, 15(6), 780-787 (ISI Thompson impact factor: 2.088)
2. Brown D.B., Damato A.L., Sutlief S., **Morcovescu S**., Park S-J., Reiff J., Shih A., Scanderbeg D.J., **2016**, *A consensus-based, process commissioning template for high-dose-rate gynecologic treatments*, Brachytherapy, 15(5), 570-577 (ISI Thompson impact factor: 2.088)
3. **Morcovescu S**., Cosma C., Morton J.D., **2016**, *Dosimetrical Evaluation and clincail implementation of a strut-adjusted-volume-implant SAVI device used for accelerated partial breast irradiation*, Romanian Journal of Physics, 61(7-8), 1312-1320 (ISI Thompson impact factor: 1.398)

List of scientific papers presented at National and International Congresses and Scientific Meetings

1. **Morcovescu S.**, Cosma C., Ferenczi J., **1999**, Radon measurement from touristic underground waters in Maramureş county, Radon in the Living Environment, April 19-23, Athens, Greece, Book of Proceedings, 269-279.
2. **Morcovescu S.**, Morton J.D., Perry K., **2009**, *The SAVI 6-1 Mini APBI applicator: A unique solution for small lumpectomy cavities and skin distances*, ASTRO 51st Annual Meeting, November 1-5, 2009, Chicago, IL, Int. Journal of Radiation Oncology Biology Physics, 75, S718.
3. **Morcovescu S.**, Morton J.D., **2009**, *A comparative clincal study and dosimetry planning experience with the new Contura multi-lumen versus MammoSite single-lumen high-dose-rate balloon breast applicators under the RTOG 0413 protocol*, ABS Annual Meeting, May 31-June 2, 2009, Toronto, Canada, Brachytherapy, 8(2), S136-137.
4. **Morcovescu S.**, Morton J.D., **2009**, *The miniSAVI multicatheter accelerated partial breast irradiation applicator and its use in patients with small lumpectomy*

cavities and/or inadequate skin distance: early clinical experience, ABS Annual Meeting, May 31-June 2, 2009, Toronto, Canada, Brachytherapy, 8(2), S138.

5. **Morcovescu S.**, Morton J.D., Perry K., **2011**, *Investigation of Interfraction Variance of a SAVI6-1 Mini APBI Applicator in Patients with Reduced Chest Wall and Skin Sparing*, ASTRO 53rd Annual Meeting, October 2-6, 2011, Miami Beach, FL, USA, (poster)
6. **Morcovescu S.**, Scanderbeg D., Reiff J., Butler E., Sadeghi A., Graves Y., Huaying J., Imhoff K. Webster J., Patra P., Mohideen N., Jacob D., Mantz C., **2012**, *Dosimetric Characteristics of Strut-Based APBI Devices*, American College Radiation Oncology (ACRO) Annual Meeting, February 25, 2012, Fort. Myers, FL, (poster)
7. Hong R, Lorio V, Huaying J, Han B, Shieh E, Imhoff K, Kuske R, Quiet C, Sadeghi A, Perry K, **Morcovescu S**, Yashar C, Scanderbeg D, Graves Y, Strasser J, Dayee Jacob D, Reiff J, Komarnicky L, Mahalingam S, Webster J, Nigh S, Mohideen N, Lobo P, Farmer M, Berry M, Patra P, Mantz C, Finkelstein S, Pollock J, Butler E, Attai D, Patel R, **2012**, *Excellent/Good Cosmetic Outcomes in Patients Treated with a Strut-Based Brachytherapy Applicator (SAVI) for Accelerated Partial Breast Irradiation*, National Consortium of Breast Centers, Inc. annual meeting, March 10-14, National Consortium of Breast Centers, Inc. annual meeting, March 10-14, 2012, Las Vegas, NV (poster)
8. **Morcovescu S**, Morton J, Perry K, **2012**, *Comprehensive dosimetric evaluation of a small strut-based APBI Device: a retrospective single-institution study*, World Congress of Brachytherapy, May 10-12, 2012, Barcelona, Spain (poster)
9. Strasser J., Jacob D., Koprowski C., Attai D., Butler E., Finkelstein S., Han B., Hong R., Komarnicky L., Kuske R., Lyden M., Mahalingam S., Mantz C., **Morcovescu S.**, Nigh S., Perry K., Pollock J., Reiff J., Scanderbeg D., Yashar C., **2012**, *Accelerated partial breast irradiation using a strut-based brachytherapy device: A multi-institutional initial report on acute and late toxicity with greater than 24-month follow-up*, Breast Cancer Symposium, September 13-15, 2012, San Francisco, CA (poster)
10. Perry K, Attai D, Finkelstein SE, Han B, Hong R, Kuske R, Lyden M, Mahalingam S, Mantz C, **Morcovescu S**, Nigh S, Pollock J, Reiff J, Scanderbeg D, Strasser J, Yashar C., **2013**, *Outcomes for Accelerated Partial Breast irradiation with a strut-based brachytherapy applicator: 320 patients with 3-year median follow up*, American Society of Breast Surgeons 14th annual meeting, May 1-5, 2013, Chicago, IL (poster)
11. Reiff J. E., Scanderbeg D., **Morcovescu S.**, Butler E., Imhoff K., **2013**, *Dosimetry of 108 Strut-Based Accelerated Partial Breast Irradiation (APBI) Treatments With Applicator Distance Less Than 7 mm from Both the Skin and Ribs*, American Association of Physicists in Medicine (AAPM) 55th annual meeting, August 4-8, 2013, Indianapolis, IN
12. Einck J.P., Scanderbeg D., Kuske R., Hong R., Han B., Perry K., Reiff J., Mahalingam S., Nigh S., Strasser J., Mantz C., Pollock J., **Morcovescu S,** Komarnicky L, Finkelstein S., Yashar C., **2013**, *Accelerated partial breast*

irradiation using strut-based brachytherapy in ductal carcinoma in situ patients: A report on 321 patients with median 25-month follow up. Data updated for 284 patients with median 27-month follow up, Breast Cancer Symposium, September 7-9, 2013, San Francisco, CA (poster)

13. Reiff J. E., Scanderbeg D., **Morcovescu S.**, Butler E., Imhoff K., **2013**, *Dosimetric analysis of 1007 Strut-based APBI treatments*, American Society of Radiation Oncology (ASTRO) 55th annual meeting, September 22-25, 2013, Atlanta, GA (poster)
14. **Morcovescu S.**, Morton J.D., Boleware Y.E., Kerri P., **2014**, *Clinical experience with a miniature accelerated partial breast irradiation device: a 5-year single institution comprehensive study*, American Brachytherapy Society (ABS) Annual meeting, April 3-5, 2014, San Diego, CA , Brachytherapy, 13, S82.
15. Yock A.D., Reiff J.E., **S. Morcovescu**, D. Scanderbeg, **2015**, *Treatment time nomogram for strut-based accelerated partial breast applicators*, American Association of Physicists in Medicine (AAPM) 57th annual meeting, July 11-16, 2015, Anaheim, CA (poster)
16. **Morcovescu S.**, Morton J.D., **2016**, *The use of a SAVI strut-based device in the boosting of a stenotic distal vagina*, World Congress of Brachytherapy, June 27-29, 2016, San Francisco, CA, Brachytherapy 15, S132.

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