



*Ain Shams University Hospitals  
Department of Clinical Oncology  
& Nuclear Medicine*

# *Accelerated Partial Breast Irradiation (3-D conformal) For Stage I and Stage II Breast Carcinoma*

*A Thesis Submitted For Partial Fulfillment of M.D Degree in  
Clinical Oncology and Nuclear Medicine*

*Presented By*

*Ahmed Ali Ahmed Badran*

*M.Sc in Radiation Oncology and Nuclear Medicine  
Faculty of Medicine Ain- Shams University*

*Supervised By*

*Dr. Soheir Sayed Sayed Ismail*

*Professor of Clinical Oncology and Nuclear Medicine Faculty of  
Medicine, Ain Shams University*

*Dr. Hussein Abdel-Alim Boushnak*

*Professor of general surgery & surgical Oncology Faculty of  
Medicine,  
Ain Shams University*

*Dr. Amin El-Sayed Amin Ahmed*

*Assistant Professor of Radiation Physics, Faculty of Medicine,  
Ain Shams University*

*Dr. Nagy Samy Gobran*

*Lecturer of Clinical Oncology and Nuclear Medicine Faculty of  
Medicine, Ain Shams University*

---

*Faculty of Medicine  
Ain Shams University*

**2011**



مستشفيات جامعة عين شمس  
قسم علاج الأورام والطب النووي

# العلاج الإشعاعي الجزئي المتسارع (ثلاثي الأبعاد) لأورام الثدي

رسالة مقدمة

توطئة للحصول على درجة الدكتوراه في علاج الأورام بالإشعاع والطب النووي

من الطبيب/ أحمد علي أحمد بدران

ماجستير في علاج الأورام بالإشعاع والطب النووي  
كلية الطب- جامعة عين شمس

تحت إشراف

الدكتورة/ سهير سيد سيد إسماعيل

أستاذ ورئيس قسم علاج الأورام بالإشعاع والطب النووي  
كلية الطب- جامعة عين شمس

الدكتور/ حسين عبد العليم بشناق

أستاذ الجراحة العامة و جراحة الاورام  
و وكيل كلية الطب- جامعة عين شمس

الدكتور/ أمين السيد أمين أحمد

أستاذ مساعد الفيزياء الإشعاعية  
كلية الطب- جامعة عين شمس

الدكتور/ ناجي سامي جبران

مدرس علاج الأورام بالإشعاع والطب النووي  
كلية الطب- جامعة عين شمس

---

كلية الطب

جامعة عين شمس

2011

## **List of tables**

	<b><i>Page</i></b>
<b><i>Table (1):</i></b> Estimated incidence, mortality and prevalence worldwide, 2002	<b><i>7</i></b>
<b><i>Table (2):</i></b> Characteristics of breast cancer subtypes defined by gene expression profiles	<b><i>16</i></b>
<b><i>Table (3):</i></b> Prognostic factors in patients in breast cancer	<b><i>27</i></b>
<b><i>Table (4):</i></b> Choice of treatment modalities according to HER-2 and endocrine response	<b><i>31</i></b>
<b><i>Table (5):</i></b> Trials between Lumpectomy and whole breast RT vs. mastectomy	<b><i>36</i></b>
<b><i>Table (6):</i></b> Spatial pattern of ipsilateral breast relapse (IBTR) in patients treated with breast conserving surgery plus whole breast radiotherapy. a 607 treated breasts.b 1 patient had an unclassifiable failure.c 2% unclear; location was reported for the 130 patients (out of 136) that could be classified according to location, pathology and flow cytometry	<b><i>85</i></b>
<b><i>Table (7):</i></b> Ipsilateral breast tumour relapse (IBTR), elsewhere failure and contralateral breast cancer (CLBC) rates after breast conservation surgery (BCS) and whole breast radiotherapy (WBRT). a First event.b Average. c Radiotherapy arm.d Alone.e Radiotherapy plus placebo arm.f IBTR not in the area of the original tumour (see previous table for definitions used in each study).g Calculated 25% of the total IBTR rate	<b><i>86</i></b>
<b><i>Table (8):</i></b> Patients “suitable” for APBI if all criteria are present	<b><i>92</i></b>

<b>Table (9):</b> “Cautionary” group: Any of these criteria should invoke caution and concern when considering APBI	<b>93</b>
<b>Table (10):</b> Patients “unsuitable” for APBI outside of a clinical trial if any of these criteria are present	<b>94</b>
<b>Table (11):</b> A comparison of the common APBI modalities for prescription. Point, total dose, fractionation/dose-rate, and biological effective dose (BED)	<b>149</b>
<b>Table (12):</b> Comparison of the current available APBI techniques (adapted from Sarin (2007), MIB = multicatheter Interstitial brachytherapy, IORT =intraoperative radiation therapy, RCT = randomized Clinical trials, OAR organ at risk	<b>150</b>
<b>Table (13):</b> Types of accelerated fractionation	<b>158</b>
<b>Table (14):</b> EORTC Cosmetic scoring criteria (Aaronson et al., 1988) and Common Terminology Criteria for Adverse Events (CTCAE, 2006)	<b>183</b>
<b>Table (15):</b> Common Terminology Criteria for Adverse Events v3.0 Cardiac toxicity	<b>184</b>
<b>Table (16):</b> RTOG/EORTC grading criteria for acute radiation toxicity (Cox et al., 1995)	<b>185</b>
<b>Table (17):</b> RTOG/EORTC late radiation morbidity grading criteria (Cox et al., 1995)	<b>186</b>
<b>Table (18):</b> Age distribution in the studied groups	<b>188</b>
<b>Table (19):</b> Tumour size in the studied groups	<b>189</b>
<b>Table (20):</b> Lymph node status in the studied groups	<b>190</b>

---

<b><i>Table (21):</i></b> Stage distribution among the studied groups	<b><i>191</i></b>
<b><i>Table (22):</i></b> Tumour side in the studied groups	<b><i>192</i></b>
<b><i>Table (23):</i></b> Hormonal receptor status and Her2neu status	<b><i>194</i></b>
<b><i>Table (24):</i></b> HER2-neu status among the studied groups	<b><i>195</i></b>
<b><i>Table (25):</i></b> Breast size among the studied groups	<b><i>196</i></b>
<b><i>Table (26):</i></b> Acute pulmonary toxicity in the studied groups	<b><i>197</i></b>
<b><i>Table (27):</i></b> Acute skin toxicity in the studied group	<b><i>199</i></b>
<b><i>Table (28):</i></b> Late pulmonary morbidity in the studied groups	<b><i>201</i></b>
<b><i>Table (29):</i></b> Late cardiac adverse events in the studied groups	<b><i>202</i></b>
<b><i>Table (30):</i></b> Late skin morbidity in the studied groups	<b><i>203</i></b>
<b><i>Table (31):</i></b> Baseline cosmetic scoring in the studied groups	<b><i>204</i></b>
<b><i>Table (32):</i></b> Post- treatment cosmetic scoring in the studied groups	<b><i>206</i></b>
<b><i>Table (33):</i></b> Local recurrence in the studied groups	<b><i>210</i></b>
<b><i>Table (34):</i></b> Comparative characteristics of the accelerated partial breast irradiation (APBI) and whole breast radiotherapy (WBRT) groups	<b><i>230</i></b>
<b><i>Table (35):</i></b> DOSIMETRIC EVALUATION	<b><i>231</i></b>

## **List of figures**

***Page***

<b><i>Figure (1):</i></b> The global burden of breast cancer in 2002: age-standardized incidence rates per 100.000	<b>9</b>
<b><i>Figure (2):</i></b> A. Magnetic resonance imaging (MRI)–detected ductal carcinoma in situ (DCIS). B. maximum intensity projection (MIP) image of the left breast with CAD stream.	<b>45</b>
<b><i>Figure (3):</i></b> Patient positioning for treatment of the intact breast therapeutic applications of radiation	<b>49</b>
<b><i>Figure (4):</i></b> Patient positioning and treatment fields for treating the intact breast using a three-field isocentric technique	<b>49</b>
<b><i>Figure (5):</i></b> A. medial and B. lateral tangent fields	<b>50</b>
<b><i>Figure (6):</i></b> Radiation Treatment of Cancer in the Left Breast.	<b>51</b>
<b><i>Figure (7):</i></b> A. External beam radiation therapy in the prone position. B. Dedicated treatment board for the treatment of breast cancer in the prone position.	<b>53</b>
<b><i>Figure (8):</i></b> Three-dimensional treatment planning (3D-CRT) with visualization at all planes through the breast tissue, tumor bed, and cardiac and pulmonary tissues.	<b>56</b>
<b><i>Figure (9):</i></b> A diagram showing target definition	<b>72</b>

<b>Figure (10):</b> External beam accelerated partial breast irradiation prescribing dose to the lumpectomy cavity plus a margin	<b>81</b>
<b>Figure (11):</b> Target definition	<b>96</b>
<b>Figure (12):</b> CT Scan of Breast Cancer Pateint	<b>99</b>
<b>Figure (13):</b> Illustration of how each point of interest (POI) was defined.	<b>104</b>
<b>Figure (14):</b> Represents the volume of the second lumpectomy cavity excluded from the first before and after adjusting the second lumpectomy cavity according to the calculated clip point of interest movement.	<b>106</b>
<b>Figure (15):</b> A diagram showing techniques for partial breast irradiation	<b>107</b>
<b>Figure (16):</b> Multicatheter interstitial brachytherapy.	<b>109</b>
<b>Figure (17):</b> A diagram showing brachytherapy	<b>110</b>
<b>Figure (18):</b> Brachytherapy planning	<b>112</b>
<b>Figure (19):</b> MammoSite radiation therapy system	<b>115</b>
<b>Figure (20):</b> MammoSite radiation therapy system. External appearance and sagittal view of balloon with dosimetric target coverage.	<b>116</b>
<b>Figure (21):</b> Three-dimensional rendering of applicator surface and prescription dose cloud in balloon intra-cavitary breast brachytherapy.	<b>117</b>
<b>Figure (22):</b> Axxent electronic brachytherapy, balloon applicator (courtesy of Xoft)	<b>119</b>
<b>Figure (23):</b> Axxent electronic brachytherapy, controller front view (courtesy of Xoft)	<b>120</b>

<b>Figure (24):</b> Axxent electronic brachytherapy, HDR X-ray source (courtesy of Xoft)	<b>121</b>
<b>Figure (25):</b> Different sizes of SAVI with peripheral struts expanded (courtesy of Cianna Medical)	<b>125</b>
<b>Figure (26):</b> ClearPath device (a) the base detached (b) a cap placed over the HDR channels (courtesy of North America Scientific)	<b>126</b>
<b>Figure (27):</b> PBSI implantation device	<b>129</b>
<b>Figure (28):</b> The seeds are loaded into the needles such that they can all be implanted at a plane perpendicular to the tip of the fiducial needle a. needle retraction is necessary and measured from the bottom of the fiducial needle b	<b>130</b>
<b>Figure (29):</b> 3D CT images taken immediately (a) and two months (b) postimplantation. The seeds show limited motion, and coalesce. As a result, the implants get hotter but the target coverage is improved	<b>133</b>
<b>Figure (30):</b> Various spherical applicators with diameters ranging from 1.5 to 5 cm used in the intrabeam device	<b>136</b>
<b>Figure (31):</b> Hard-docking system	<b>139</b>
<b>Figure (32):</b> Radiation treatment	<b>140</b>
<b>Figure (33):</b> 3D Conformal External Beam APBI	<b>141</b>
<b>Figure (34):</b> CT simulator	<b>144</b>
<b>Figure (35):</b> a 3 3D conformal APBI (cavity and CTV). b I (cavity, CTV, and PTV) c cavity, CTV, PTV, and PTV_EVAL)	<b>145</b>



<b>Figure (36):</b> Three-dimensional conformal external beam radiotherapy. Four field beam arrangement and conformal, homogeneous dose coverage of the target.	<b>146</b>
<b>Figure (37):</b> <b>Panel A</b> shows a cancer in the upper outer quadrant of the left breast. <b>Panel B</b> shows biologic effects of ionizing radiation on the tumor cells and on a normal stromal cell.	<b>153</b>
<b>Figure (38):</b> Age distribution in the studied groups	<b>188</b>
<b>Figure (39):</b> Tumour size in the studied groups	<b>189</b>
<b>Figure (40):</b> Lymph node status in the studied groups	<b>190</b>
<b>Figure (41):</b> Stage distribution among the studied groups	<b>191</b>
<b>Figure (42):</b> Tumour side in the studied groups	<b>192</b>
<b>Figure (43):</b> Hormone receptor status in the studied groups	<b>194</b>
<b>Figure (44):</b> Breast size among the studied groups	<b>196</b>
<b>Figure (45):</b> Acute pulmonary toxicity in the studied groups	<b>197</b>
<b>Figure (46):</b> DVH of acute pulmonary toxicity patient	<b>198</b>
<b>Figure (47):</b> Acute skin toxicity in the studied groups	<b>200</b>
<b>Figure (48):</b> left breast treated by WBI, Dmax skin 104%	<b>200</b>
<b>Figure (49):</b> Late pulmonary morbidity in the studied groups	<b>201</b>
<b>Figure (50):</b> Grade of cardiac adverse events in the studied groups	<b>202</b>
<b>Figure (51):</b> Late skin morbidity in the studied groups	<b>203</b>

<b>Figure (52):</b> Baseline cosmetic scoring in the studied groups	<b>204</b>
<b>Figure (53):</b> Post- treatment cosmetic scoring in the studied groups	<b>206</b>
<b>Figure (54):</b> An example of an excellent cosmetic result post-treatment photo in a patient in group A	<b>207</b>
<b>Figure (55):</b> An example of a good cosmetic result in a patient in group A. Pre-treatment photo to the left and post-treatment photo to the right	<b>207</b>
<b>Figure (56):</b> An example of a good cosmetic result in a patient in the conventional group B. Pre-treatment photo above and post-treatment photo below	<b>208</b>
<b>Figure (57):</b> Late Grade 3 fibrosis at 2 years of follow-up	<b>209</b>
<b>Figure (58):</b> Local recurrence in the studied groups	<b>210</b>
<b>Figure (59):</b> Digitally reconstructed skin-rendered view that shows projections of two minitangents field used	<b>212</b>
<b>Figure (60)</b> Three-dimensional graphic reconstruction of five beam-eye views for 3D conformal APBI.	<b>213</b>
<b>Figure (61):</b> Representative dosimetry for a three-field, partial-breast irradiation treatment plan with axial, sagittal, and coronal views	<b>213</b>
<b>Figure (62):</b> Represents 3D conformal APBI in right breast lesion	<b>215</b>
<b>Figure (63A):</b> Dose distribution in left breast treated in arm A	<b>216</b>

<b>Figure (63B):</b> Plane summery sheet	<b>217</b>
<b>Figure (63C):</b> Dose volume histogram	<b>218</b>
<b>Figure (64):</b> Clinical target and Planning target volume <sub>95</sub> and volume <sub>107</sub>	<b>221</b>
<b>Figure (65):</b> Clinical target and Planning target volume <sub>95</sub>	<b>222</b>
<b>Figure (66):</b> Clinical target and Planning target volume <sub>107</sub>	<b>223</b>
<b>Figure (67):</b> Ipsilateral breast volume <sub>35</sub>	<b>224</b>
<b>Figure (68):</b> Ipsilateral breast volume <sub>60</sub>	<b>224</b>
<b>Figure (69):</b> Ipsilateral breast volume <sub>35</sub> and volume <sub>60</sub>	<b>225</b>
<b>Figure (70):</b> Ipsilateral lung volume <sub>15</sub>	<b>226</b>
<b>Figure (71):</b> Ipsilateral lung volume <sub>20</sub>	<b>226</b>
<b>Figure (72):</b> Ipsilateral lung volume <sub>15</sub> and volume <sub>20</sub>	<b>227</b>
<b>Figure (73):</b> Heart volume <sub>5</sub>	<b>228</b>
<b>Figure (74):</b> Normal tissue complication probability	<b>229</b>
<b>Figure (75):</b> Equivalent uniform dose	<b>229</b>

### **List of abbreviations**

<b>(3D-CRT)</b>	Three-dimensional conformal radiation therapy
<b>(a/b (<math>\alpha/\beta</math>))</b>	Alpha over beta ratio
<b>(ABS)</b>	American Brachytherapy Society
<b>(AJCC)</b>	American Joint Committee of Cancer
<b>(APBI)</b>	Accelerated Partial breast irradiation
<b>(ASBS)</b>	American Society of breast Surgeons
<b>(ASCO)</b>	American Society of Clinical Oncology
<b>(ASCOD)</b>	Ain Shams University clinical oncology department
<b>(ASTRO)</b>	American Society for Radiation Oncology
<b>(ATAC)</b>	Anastrozole, Tamoxifen, Alone or in Combination
<b>(BCIRG)</b>	Breast Cancer International Research Group
<b>(BCS)</b>	Breast-conserving surgery

<b>(BCT)</b>	Breast-conserving therapy
<b>(BED)</b>	Biological Effective Dose
<b>(BRCA 1,2)</b>	<b><u>B</u>reast <u>C</u>ancer susceptibility gene <u>1,2</u></b>
<b>(BV)</b>	Breast volume
<b>(CBCT)</b>	Cone-beam CT
<b>(cDNA)</b>	Complementary Deoxyribonucleic acid
<b>(CF)</b>	Conventional fractionation
<b>(CI)</b>	confidence interval
<b>(CP)</b>	Clear Path
<b>(CT)</b>	Computed tomography
<b>(CTCAE)</b>	Criteria for Adverse Events
<b>(CTV)</b>	Clinical Target Volume
<b>(DBCG)</b>	Danish Breast Cancer Cooperative Group
<b>(DCIS)</b>	Ductal Carcinoma In Situ
<b>(DFS)</b>	Disease free survival

<b>(DVH)</b>	Dose–volume histograms
<b>(EBCTCG)</b>	Eareast Cancer Trialists’ Collaborative Group
<b>(EBRT)</b>	External beam radiotherapy
<b>(EB-APBI)</b>	External -beam accelerated partial-breast irradiation
<b>(ELIOT)</b>	Electron Intraoperative Therapy
<b>(EIC)</b>	Extensive intraductal component
<b>(EORTC)</b>	European Organization for Research and Treatment of Cancer
<b>(eB)</b>	Axxent electronic brachytherapy
<b>(ER)</b>	Estrogen receptor
<b>(ER–)</b>	Estrogen receptor negative
<b>(ER+)</b>	Estrogen receptor positive
<b>(EUD)</b>	Equivalent Uniform Dose
<b>(FDA)</b>	Food and Drug Administration

<b>(GEC-ESTRO)</b>	Groupe Européen de Curiethérapie-European Society for Therapeutic Radiology and Oncology
<b>(GY)</b>	Gray
<b>(HCT)</b>	Helical CT
<b>(HAD)</b>	High-dose afterloader
<b>(HDR)</b>	High Dose Rate
<b>(HER2/neu)</b>	Human Epidermal growth factor Receptor 2
<b>(HR+)</b>	Hormonal receptor positive
<b>(IBTR)</b>	ipsilateral breast tumor recurrence
<b>(IDC)</b>	Invasive Duct carcinoma
<b>(IDL)</b>	Iso-dose Line
<b>(ILC)</b>	Invasive lobular carcinoma
<b>(IMRT)</b>	Intensity Modulated Radiotherapy
<b>(IORT)</b>	Intra-operative electron beam Radiotherapy
<b>(KV)</b>	Kilo- voltage