Valutazione tossicità nel trattamento radiante ipofrazionato con concomitant boost settimanale in pazienti con diagnosi di carcinoma mammario sottoposte a chirurgia conservativa

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LINEE GUIDA AIRO 2009

Dopo chirurgia conservativa la mammella può essere trattata impiegando un frazionamento convenzionale (1,8-2Gy/die, in 5 frazioni settimanali fino alla dose totale di 50,0-50,4 Gy) o schemi ipofrazionati, la cui equivalenza, in termini di efficacia e tossicità, è stata inizialmente dimostrata da uno studio randomizzato canadese[1], i cui risultati sono stati aggiornati allo scorso congresso ASTRO, con un follow-up di 12 anni.


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Long-Term Results of Hypofractionated Radiation Therapy for Breast Cancer

Timothy J. Whelan, B.M., B.Ch., Jean-Philippe Pignol, M.D., Mark N. Levine, M.D., Jim A. Julian, Ph.D., Robert MacKenzie, M.D., Sameer Parpia, M.Sc., Wendy Shelley, M.D., Laval Grimard, M.D., Julie Bowen, M.D., Himu Lukka, M.D., Francisco Perera, M.D., Anthony Fyles, M.D., Ken Schneider, M.D., Sunil Gulavita, M.D., and Carolyn Freeman, M.D.

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0360-3016/$–see front matter

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CLINICAL INVESTIGATION **Breast**

FRACTIONATION FOR WHOLE BREAST IRRADIATION: AN AMERICAN SOCIETY FOR RADIATION ONCOLOGY (ASTRO) EVIDENCE-BASED GUIDELINE

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Treated with breast-conserving surgery
Age ≥50 years
pT1–2
pN0
Chemotherapy not used
Central axis inhomogeneity −7% to +7%

Conclusion: Data were sufficient to support the use of HF-WBI for patients with early-stage breast cancer who met all the aforementioned criteria. For other patients, the task force could not reach agreement either for or against the use of HF-WBI, which nevertheless should not be interpreted as a contraindication to its use.

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The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial

*The START Trialists' Group**

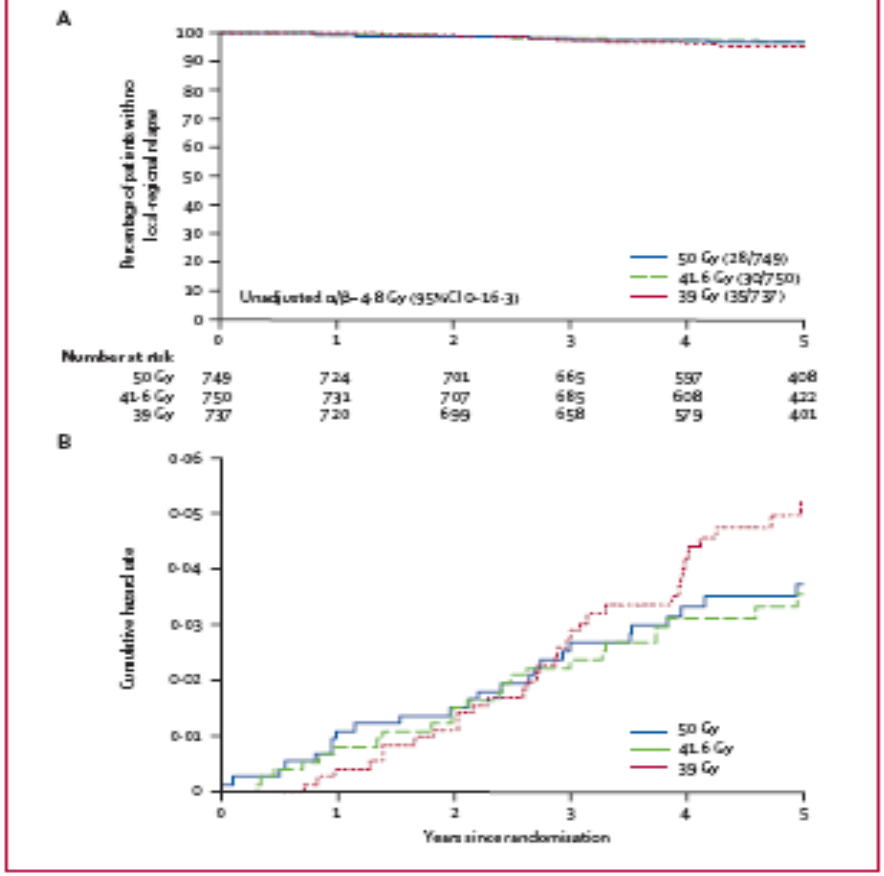


Figure 2: Kaplan-Meier plot (A) and Nelson-Aalen cumulative hazard plot (B) of local-regional tumour relapse in 2236 patients

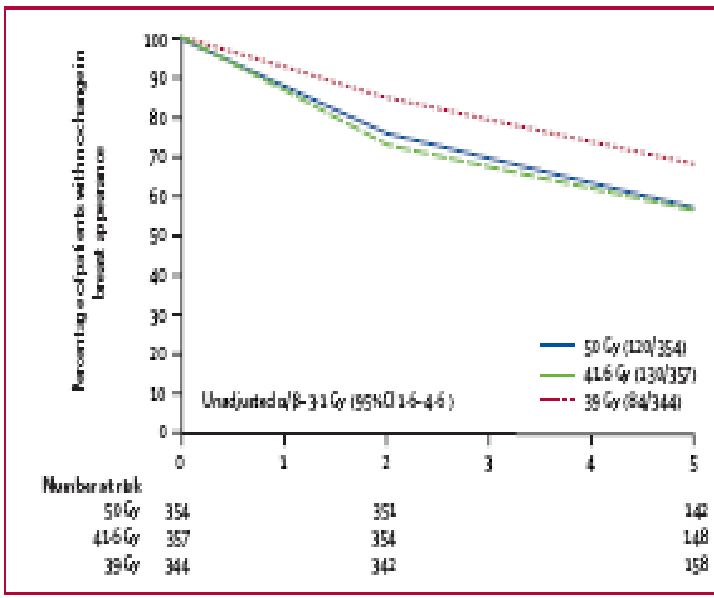
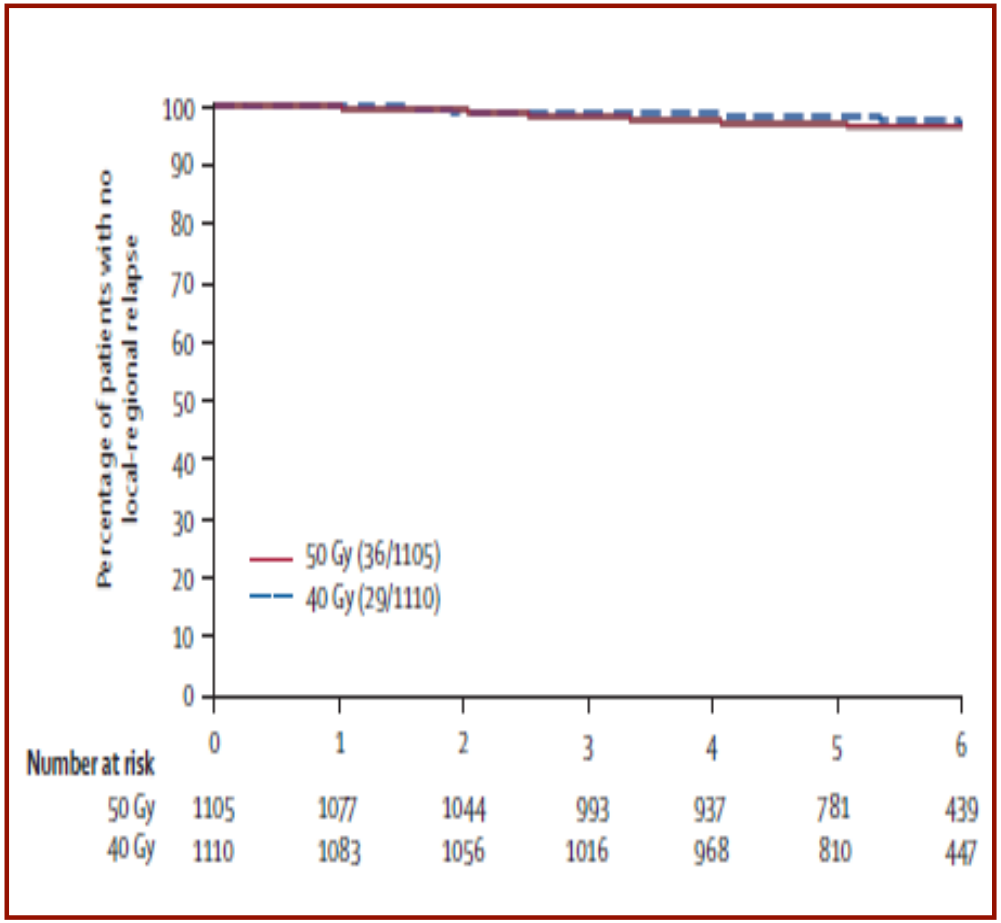


Figure 3: Kaplan-Meier plot of mild/marked change in breast appearance (photographic) in 1055 patients with breast conserving surgery

The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: a randomised trial

*The START Trialists' Group**



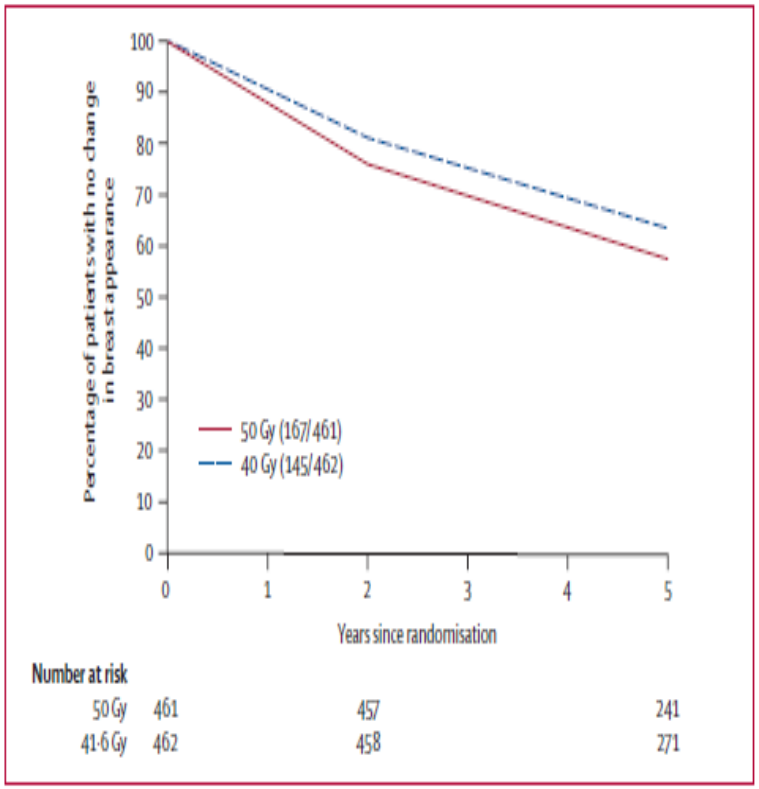
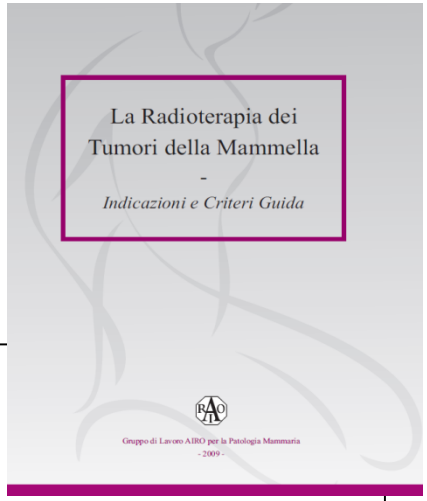


Figure 4: Kaplan-Meier plot of mild/marked change in breast appearance (photographic) in 923 patients with breast conserving surgery

LINEE GUIDA AIRO 2009



Poiché la maggior parte delle recidive locali è documentata in corrispondenza o nelle immediate vicinanze del letto tumorale, al fine di ridurne l'incidenza, l'erogazione di un sovradosaggio al letto operatorio (boost) è pratica routinaria presso la maggior parte dei Centri di Radioterapia.
L'esecuzione del boost è soprattutto raccomandata in pazienti di età inferiore a 40 anni ed in quelle ad elevato rischio di recidiva.

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PRINCIPLES OF RADIATION THERAPY

Whole Breast Radiation:
Target definition includes the majority of the breast tissue, and is best done by both clinical assessment and CT-based treatment planning. A uniform dose distribution and minimal normal tissue toxicity are the goals and can be accomplished using compensators such as wedges, forward planning using segments, intensity-modulated radiation therapy (IMRT), respiratory gating, or prone positioning. The breast should receive a dose of 45-50 Gy in 1.8-2 Gy per fraction, or 42.5 Gy at 2.66 Gy per fraction. A boost to the tumor bed is recommended in patients at higher risk (age <50 and high-grade disease). This can be achieved with brachytherapy or electron beam or photon fields. Typical doses are 10-16 Gy at 2 Gy/fx. All dose schedules are given 5 days per week.

Chest Wall Radiation (including breast reconstruction):
The target includes the ipsilateral chest wall, mastectomy scar, and drain sites where possible. Depending on whether the patient has been reconstructed or not, several techniques using photons and/or electrons are appropriate. CT-based treatment planning is encouraged in order to identify lung and heart volumes, and minimize exposure of these organs. Special consideration should be given to the use of bolus material when photon fields are used, to ensure the skin dose is adequate.

Regional Nodal Radiation:
Target delineation is best achieved by the use of CT-based treatment planning. For the paraclavicular and axillary nodes, prescription depth varies based on the size of the patient. For internal mammary node identification, the internal mammary artery and vein location can be used as a surrogate for the nodal locations, which usually are not visible on imaging.

Dose is 50-50.4 Gy, given as 1.8-2.0 Gy fraction size (± scar boost at 2 Gy per fraction to a total dose of approximately 60 Gy); all dose schedules are given 5 days per week. If internal mammary lymph nodes are clinically or pathologically positive, radiation therapy should be given to the internal mammary nodes. Otherwise the treatment to the internal mammary nodes is at the discretion of the treating radiation oncologist. CT treatment planning should be utilized in all cases where radiation therapy is delivered to the internal mammary lymph node field.

Accelerated Partial Breast Irradiation (APBI):
Preliminary studies of APBI suggest that rates of local control in selected patients with early-stage breast cancer may be comparable to those treated with standard whole breast RT. Follow-up, however, is limited and studies are ongoing. Patients are encouraged to participate in clinical trials. If not trial eligible, per the consensus statement from the American Society for Radiation Oncology (ASTRO), patients who may be suitable APBI are women 60 y and older who are not carriers of BRCA 1/2 mutation treated with primary surgery for a unifocal T1N0 ER-positive cancer. Histology should be infiltrating ductal or a favorable ductal subtype and not associated with EIC or LCIS, and margins should be negative. Thirty-four Gy in 10 fractions delivered twice per day with brachytherapy or 38.5 Gy in 10 fractions delivered twice per day with external beam photon therapy is prescribed to the tumor bed. Other fractionation schemes are currently under investigation.

Optimizing Delivery of Individual Therapy:
It is important to individualize delivery of radiation therapy and considerations such as patient positioning (ie, prone vs. supine) during administration of radiation therapy.

Neoadjuvant chemotherapy:
Indications for radiation therapy and fields of treatment should be based on the pretreatment tumor characteristics in patients treated with neoadjuvant chemotherapy.

BOOST

(Owen 2006). Of women enrolled, 1051 (75%) were treated with a boost of 14 Gy at 90% in seven fractions. The authors did not report how many women in each arm received a boost. For women with negative margins, if the clinician felt it was appropriate, there was a sub-randomisation to boost or no boost from January 1986 to May 1994. After this, all 687 patients were offered an elective boost (see additional Table 4).

START A

10 Gy / 5 fr nel **61%,**

bilanciato nei due bracci.
Partecipanti allo studio dichiaravano prima l'intento di erogare il boost

START B

10 Gy in 5 fr con e ¯ nel **43 %,**
bilanciato nei due bracci .
Partecipanti allo studio dichiaravano prima l'intento di erogare boost

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American Society for Radiation Oncology (ASTRO) 55th Annual Meeting: Press conference, September 23, 2013.

ASTRO: 5 Radiation Oncology Practices Should Stop

Shorter Schedules in Breast Cancer

In the treatment of breast cancer, ASTRO reminds oncologists to consider shorter treatment schedules when thinking about radiotherapy as part of breast-conservation therapy in women aged 50 years or older with early stage, invasive breast cancer without considering shorter treatment schedules.

Recent studies have demonstrated that women aged 50 years or older with early stage breast cancer can have equivalent tumor control and cosmetic outcome with shorter courses of radiotherapy (approximately 4 weeks) as with longer courses, according to ASTRO press materials.

ASTRO points out that whole-breast radiotherapy decreases local recurrence and improves survival of women with invasive breast cancer treated with breast-conservation therapy.

Most studies that established this practice have utilized "conventionally fractionated" schedules that deliver therapy over 5 – 6 weeks, often followed by 1 – 2 weeks of boost therapy, the organization says.But it is time to consider shorter schedules when determining, with patients, the appropriate course of action, said Dr. Steinberg.Radiation oncologists also need to consider using simpler treatment schemes in patients with bone pain from the spread of a primary tumor, ASTRO says.Clinicians should not routinely use extended fractionation schemes (>10 fractions) for

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IPOFRAZIONAMENTO

TEMPI TRATTAMENTO INFERIORI

MAGGIORE COMPLIANCE

RIDUZIONE COSTI

RIDUZIONE LISTE D'ATTESA

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CRITERI D'INCLUSIONE

Istologia di **carcinoma mammario** asportato mediante intervento chirurgico standard di tipo **conservativo**

Età **≥ 55 anni**

Non interessamento del linfonodo sentinella o max 3 linfonodi ascellari metastastatici, dopo dissezione classica.

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CRITERI D'INCLUSIONE

Margini chirurgici negativi o solo focalmente positivi (positività limitata ad uno solo dei margini di exeresi)

Disponibilità a ripresentarsi c/o S.C. Radioterapia per le visite di **follow-up**

Possibilità di effettuare successivi **esami radiologici**

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CRITERI D'ESCLUSIONE

Gravi malattie o condizioni in grado di compromettere il trattamento

Presenza di disturbi **psichiatrici** gravi

Presenza di **collagenopatie**

Macromastia

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TRATTAMENTO

Irradiazione della mammella(Whole Breast irradiation) in**13 sedute**, **4 frazioni** alla settimana,

dose singola **300cGy**, dose totale **39 Gy**

Durante lo stesso periodo viene somministrata una dose aggiuntiva al **letto tumorale**, una sola volta alla settimana con dose singola di **100cGy** per **3** sedute totali

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CASISTICA

Gennaio 2010 → Febbraio 2013

108 pazienti

F.U. Mediano 14 months (range 3-28)

Mean age in yrs 74 (range 55-89)

Tumor classification (AJCC)

pTis	5	(4,6%)
pT1a	4	(3,7%)
pT1b	25	(23,2%)
pT1c	58	(53,7%)
pT2	15	(13,9%)
pT1mic	1	

Nodal status

Neg	96	(88,9%)
Pos	7	(6,5%)
mic	5	(4,6%)

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Proliferative index (Ki 67) %

> 15%→ 33(30,6%)

≤ 15%→ 75(69,4%)

HR status

Neg 15 (13,9%)

Pos 93 (86,1%)

Hormonal therapy → 93 (86,1%)

Chemotherapy →15 (13,9%)

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Tossicità Acuta

Grade 0	No change over baseline
Grade 1	Follicular, faint or dull erythema/epilation/dry desquamation/ decreased sweating.
Grade 2	Tender or bright erythema, patchy moist desquamation/ moderate edema
Grade 3	Confluent, moist desquamation other than skin folds, pitting edema
Grade 4	Ulceration, haemorrhage, necrosis

RTOG score

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Tossicità Tardiva (lent Soma)

	Grade 1	Grade 2	Grade 3	Grade 4
Fibrosis	Barely palpable increased density	Definite increased density and firmness	Very marked density, retraction and fixation	
Telangiectasia	< 1 cm^2	1 - 4 cm^2	>4 cm^2	
Hyperpigmentation	mild	moderate	severe	
Retraction/Atrophy	10-25%	>25-40%	>40-75%	Whole breast
Ulcer	Epidermal ≤ 1cm^2	Dermal , >1cm^2	Subcutaneos	Bone exposed, necrosis

TOSSICITA' CUTANEA

	G0	G1	G2	G3	Totale pz
Termine RT	48 (44,4%)	54 (50%)	6 (5,6%)	-	108
1 mese	68 (65,4%)	36 (34,6%)	-	-	104
6 mesi	65 (76,5%)	20 (23,5%)	-	-	85

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TOSSICITA' CUTANEA

	G0	G1	G2	G3	Totale pz
12 mesi	58 (86,6%)	9 (13,4%)	-	-	67
18 mesi	40 (87%)	6 (13%)	-	-	46
24 mesi	20(87%)	3 (13%)	-	-	23

Nessuna recidiva locale

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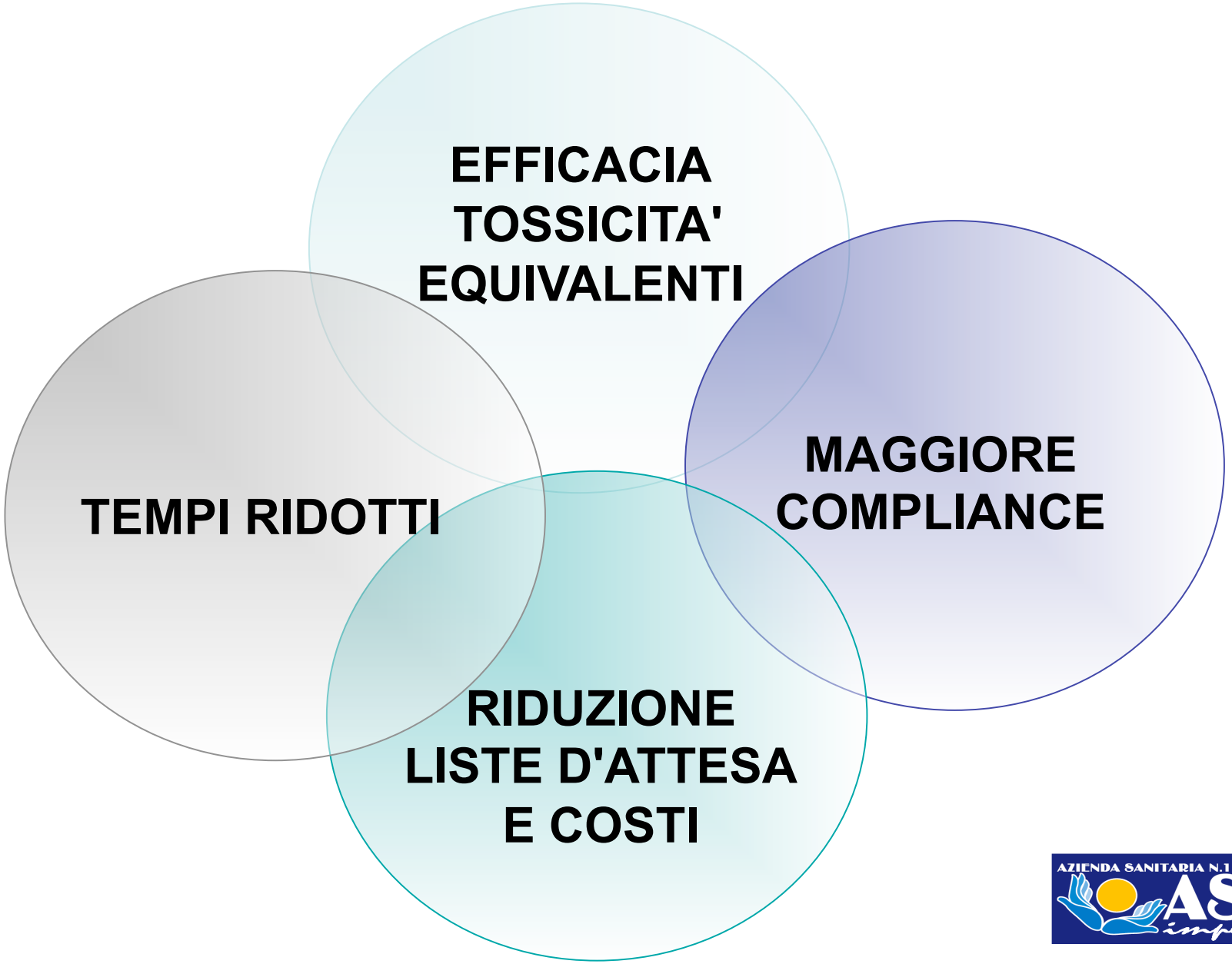
IPOFRAZIONAMENTO



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XXIII CONGRESSO

AIRO

Giardini Naxos - Taormina, 26 - 29 ottobre

Regione Siciliana - Assessorato Regionale dei Beni Culturali e dell'Identità Siciliana
Dipartimento dei Beni Culturali e dell'Identità Siciliana
Servizio Museo interdisciplinare Regionale "A. Pepoli" Trapani.