Chronic Radiation Exposure Induces Cellular Adaptive Response in Interventional Cardiologists

Gian Luigi Russo

*Istituto di Scienze dell'Alimentazione*
via Roma 64, 83100 Avellino
e-mail: glrusso@isa.cnr.it
http://www.isa.cnr.it

“DOSE-RESPONSE 2012”
The 11th Annual International Conference
April 25, 2012
University of Massachusetts, Amherst, MA
Cellular adaptive response to chronic radiation exposure in interventional cardiologists

Gian Luigi Russo 1*, Idolo Tedesco 1, Maria Russo 1, Angelo Cioppa 2, Maria Grazia Andreassi 3, and Eugenio Picano 2,3

1Institute of Food Sciences, National Research Council, Via Roma, 64, 81100 Avellino, Italy; 2Clinica Cardiologica "Monterevine", Mercogliano, Avellino, Italy; and 3Institute of Clinical Physiology, National Research Council, Pisa, Italy

Received 5 February 2011; revised 11 May 2011; accepted 6 July 2011; online publish-ahead-of-print 23 August 2011

See page 292 for the editorial comment on this article (doi:10.1093/eurheartj/ehr288)
“Friendly fire” on Interventional Cardiologists

“Not infrequently, there is a machismo disregard for radiation protection”

Rita Watson, Sayonara ALARA, Cath Cardiov Diagn, 1997

“Exposure of interventional radiologists is above and beyond every regulatory support”

(DIMOND EU Conc Action, 2001: Professional ICRP limit: 20 mSv/year)

“Lifetime extra-cancer risk of interventional cardiologists and electrophysiologists: 1 in 100-1 in 250 (100-200 mSv) after 11-25 years of cath lab” (Venneri L. et al, Am Heart J 2009)

Vano E et al, BJR 1998
DNA Damage in Interventional Cardiologists

Andreassi et al, FASEB J 2005

Group I (exposed) vs. Group II (non-exposed) with p=0.001

Gian Luigi Russo

Amherst, MA 04/25/2012
DNA Damage in Interventional Cardiologists

![Photographs of monozygotic twins. (B) Type of structural chromosomal aberrations/500 metaphases for each twin.](image)

<table>
<thead>
<tr>
<th>Chromosomal alterations</th>
<th>Twin 1 (unexposed)</th>
<th>Twin 2 (exposed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chromatid breaks</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>Chromosome breaks</td>
<td>1</td>
<td>7</td>
</tr>
<tr>
<td>Acentric Fragments</td>
<td>/</td>
<td>2</td>
</tr>
<tr>
<td>Exchanges (quadriradial)</td>
<td>/</td>
<td>1</td>
</tr>
<tr>
<td>Dicentric chromosome</td>
<td>/</td>
<td>3</td>
</tr>
<tr>
<td>Total aberrant cells/500</td>
<td>6</td>
<td>16</td>
</tr>
<tr>
<td>Frequency (%)</td>
<td>1.2</td>
<td>3.2</td>
</tr>
</tbody>
</table>
"LDR generate risk factors that are lower than predicted by the LNT, that these risks do not exist, or even that low doses of radiation may even be beneficial (linear model with a threshold)"
Gene Response

Adaptive vs Non-Adaptive

- DNA Repair
- Stress Response
- Apoptosis
- Cell Cycle

Coleman et al 2005
Study Design

10 EXPOSED CARDIOLOGISTS

Oxidative stress markers
Apoptotic markers

10 UNEXPOSED SUBJECTS
## Characteristics of the Examinees

<table>
<thead>
<tr>
<th></th>
<th>Unexposed (Group I)</th>
<th>Exposed (Group II)</th>
<th>P-valu</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>35 ± 3</td>
<td>38 ± 5</td>
<td>0.530</td>
</tr>
<tr>
<td>Gender [n (%)]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (80)</td>
<td>10 (100)</td>
<td>1.00</td>
</tr>
<tr>
<td>Female</td>
<td>2 (20)</td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Body mass index</td>
<td>22 ± 2</td>
<td>26 ± 2</td>
<td>0.010</td>
</tr>
<tr>
<td>Alcohol consumption</td>
<td>0/10</td>
<td>1/10</td>
<td>1.00</td>
</tr>
<tr>
<td>Smoking habit</td>
<td>1/10</td>
<td>2/10</td>
<td>1.00</td>
</tr>
<tr>
<td>Dietary style</td>
<td>National cuisine</td>
<td>National cuisine</td>
<td></td>
</tr>
<tr>
<td>Supplements</td>
<td>No</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Dose (mSv/year)</td>
<td>0</td>
<td>4.7 ± 3.2</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0</td>
<td>1.2–8.3</td>
<td></td>
</tr>
<tr>
<td>Years of exposure</td>
<td>0</td>
<td>10 ± 6</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0</td>
<td>3–19</td>
<td></td>
</tr>
<tr>
<td>Number of procedures</td>
<td>0</td>
<td>525 ± 100</td>
<td></td>
</tr>
<tr>
<td>Range</td>
<td>0</td>
<td>250–750</td>
<td></td>
</tr>
</tbody>
</table>
Oxidative Stress in non-Exposed vs Exposed
Antioxidant Power in Serum

Antioxidant Power (Ascorbic Acid Eq [µM])

unexposed  exposed

0.55
SOD in non-Exposed vs Exposed

ROS

\[ \text{O}_2^- \xrightarrow{\text{SOD}} \text{H}_2\text{O}_2 \]

\[ 2\text{H}^+ + 2\text{O}_2^- \rightarrow \text{H}_2\text{O}_2 + \text{O}_2 \]

Metal Chelators

\[ \text{OH}^- \]

\[ \text{ROO}^- \rightarrow \text{RO}^- \]

Oxidative damage
DNA
Lipids
Proteins

Klucinski et al., 2008
**SOD in non-Exposed vs Exposed**

ROS

$\text{O}_2^- \xrightarrow{\text{SOD}} \text{H}_2\text{O}_2 \xrightarrow{\text{catalase}} \text{H}_2\text{O} + \text{O}_2$

$2\text{H}^+ + 2\text{O}_2^- \rightarrow \text{H}_2\text{O}_2 + \text{O}_2$

$\text{Fe}^{2+}$

Metal Chelators

$\text{OH}^-$

$\text{ROO}^- \rightarrow \text{RO}^-$

Oxidative damage
- DNA
- Lipids
- Proteins

Graph:
- Catalase Activity (μmol/min/mg)
  - Unexposed: 250
  - Exposed: 190

Gian Luigi Russo
Amherst, MA 04/25/2012
GSH in Erythrocytes of non-Exposed vs Exposed

\[ 2\text{H}_2\text{O} \rightarrow \text{GSH} \] (reduced) \[ \text{GSSG} \] (oxidized) \[ \text{NADP}^+ \rightarrow \text{NADPH} \]

ROS

\[ \text{O}_2^- \rightarrow \text{SOD} \rightarrow \text{H}_2\text{O}_2 \]

Metal Chelators

\[ \text{Fe}^{2+} \rightarrow \text{OH}^- \]

Detoxification

GSH peroxidase (GPx)
GSH transferase (GST)

lipid hydroperoxides
GSH in Erythrocytes of non-Exposed vs Exposed

GSH (mM)

unexposed  exposed

0.003
ROS in Erythrocytes of non-Exposed vs Exposed
Conclusion - 1

UNEXPOSED
Antioxidant Defense (e.g., GSH)

EXPOSED
GSH ↑

Cellular Redox Homeostasis

ROS (H₂O₂, O₂•, OH•)

LDR

ROS ↑
Apoptotic Response in Interventional Cardiologists

Louagie et al., Cell Biol Int. 1999; 23:611-7

Gian Luigi Russo

Amherst, MA 04/25/2012
In interventional cardiologist chronic exposure to LDR induces at least two physiological adaptive responses: enhanced antioxidant defence (GSH levels), increased baseline level of caspase-3 activity.

The biochemical remodelling induced by chronic LDR exposure in interventional cardiologists might even overturn into a survival advantage.

The biochemical remodelling induced by chronic LDR exposure might contribute to generate new guidelines in interventional cardiology, which are currently based, almost exclusively, on minimizing radiation exposure by implementing safety measures and protection devices.
Healthy Cath Lab STUDY

- Invasive cardiologists today have a unique opportunity to clarify the effects of chronic LDR.
- This large study is being conducted in Italy to address this question.
- It is done by interventional cardiologists on interventional cardiologists and for interventional cardiologists.
- The aim is to clarify the cancer and non-cancer effects of chronic low dose radiation exposure.
Acknowledgments

ISA-CNR
Gian Luigi Russo
IdoloTedesco
Maria Russo

IFC-CNR
Maria Grazia Andreassi
Eugenio Picano

Gaetano Mottola
Angelo Cioppa
Eugenio Picano
Acknowledgments -2

ISA-CNR

Idolo Tedesco
Maria Russo
Carmela Spagnuolo
Roberta Iannitti
Annunziata Nappo
My father was a health physicist and assures me that radiation is not hazardous

....Let’s hope not ....... !!!