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ONE CENTURY OF RADON THERAPY

Klaus Becker

(Vice-President, Radiation Science & Health, Boothstr. 27, D-12207 Berlin/Germany,

(e-mail prof.dr.klaus.becker@t-online.de <mailto:prof.dr.klaus.becker@t-online.de>)

Abstract.

Supplementing a recent review "Health Effects of High Radon Environments in Central Europe: Another Test for thje LKNR Hypothesis (Becker 2003), this review of medical radon applications (in particular for the treatment of painful degenerative joint and spine diseases) covers mainly the first century of large-scale use and scientific studies on this subject since the discovery of radon. Most of the studies and experiences originated in Europe, in particular Germany, Austria, and the former USSR. They have in common that they are not well known in the anglophonic scientific literature, where radon therapy is still frequently considered a placebo-type "traditional medicine", and not be compared with the drugs such as nonsteroid antirheumatics. Hopwever, based on the substantial experiences as reflected in more than one thousand papers, mostly in peer-reviewed scientific journals, on this subject, radon therapy by inhalation or bathes has been established as an evidence-based effective treatment not only by empirical experience in different times and cultures,, but also in randomized clinical double-blind studies. It should be further explored as an effective alternative to the use of pharmaca. Unlike radon, drugs cause serious side-effects, with more than ten thousand annual casualties. The benefits in the adequate use of low-dose radon exposures far exceed the hypothetical lung cancer risk attributed to the inhalation of low radon concentrations. Further research could provide better understanding of the mechanism of the stimulating radon effects on the body's defense systems.

1. **Introduction.**

About a century ago, the therapeutic use of the newly discovered gaseous "emanations" from the radioactive elements radium and thorium commenced in Central Europe on a rapidly expanding scale. However, relatively little is known in the English-language scientific and popular literature about the therapeutic use of Rn-222, the noble gas which is a decay product of Ra-226 (with a varying contribution of its further radioactive decay products known as radon daughters products, or progeny, in this review summarized as "radon"). Instead, reports about the potential health hazards of radon in mines and homes, claimed to cause large numbers of lung cancers, dominated in recent decades the scientific and popular literature (for reviews, see Becker 2001, Becker 2002, Becker 2003). Neither a book on radon politics in the USA (Cole 1993), nor the Radon Literature Survey Series of the U.S. DOE (e. g. Radon Epidemiology

1988), and various reports on radon effects by ICRP, NCRP, BEIR IV, BEIR VI, or UNSCEAR even mention biopositive radon effects; and in a recent Letter exchange in a leading radiation protection journal (Eichholz, and Huber and Ennemoser 2002) the term “radon spa” even has been suggested to be an “oxymoron”.

It is the purposes of this review to provide a compilation for interested readers who are not familiar with the substantial experiences and literature in Europe, where radon therapy, in particular for the treatment of painful inflammatory and degenerative joint and spine diseases, has long been valued, with an overview of the information and experience which has accumulated in more than one thousand scientific publications, mostly in peer-reviewed medical journals.

There have been several stages in the history of radon therapy, including the times when it was only indirectly known by its positive health effects millennia ago; the first decades of scientific exploration of its properties and concentration in various sources of mineral waters after its discovery, and uses in old or newly established therapeutic facilities. During this period, the terms “radium” and “radon” were used frequently as synonyms, resulting in names such as “Radiumbad” in German-speaking countries. Soon the careful medical supervision of the treatment procedures and their results was initiated with many reports on the results, thus narrowing the sometimes very wide spectrum of applications essentially to the first known uses, namely painful rheumatic and arthritic joint and spine diseases. In particular in the former Soviet Union, radon therapy were studied and used, with numerous publications on this subject and over a million of annual treatments. However, some other applications, such as the use of sealed capillaries filled with radon for local tumour treatment in the USA, or radium compresses for external treatment of various ailments, are not covered in this review.

Occasionally, doubts about the merits of radon therapy have been expressed and are still common in parts of the medical community, e.g. in comparing it with various types of “traditional”, “natural”, or “folk medicine” such as acupuncture, etc., as used for many centuries in Eastern Asia and Africa, or homeopathy, mostly in Europe. Some of such cures have been demonstrated in serious animal and human studies as being effective, while most of them clearly belonged into the category of “alternative medicine” based on the firm believe in the desired effect. Radon therapy should not be confused with this type of treatments, as well as with

- the in many cultures traditional use of hot springs for increasing the general feeling of well-being and relieving various old-age problems (in Northern Japan, even monkeys enjoy hot springs in winter),
- the “speleotherapy” of bronchial asthma in the allergen-free atmosphere of NaCl or KCl salt mines, with a long tradition in Central and Southeastern Europe (e.g. the Wielizka mine near Krakov), and

- the old habit of adding herbs, spices, salts, etc., to bathing or drinking water assumed to improve their beneficial effects.

As it turned out, radon did not belong into this category, and in fact helped to prevent the serious side effects of the pharmaceutical treatment of painful rheumatic and arthritic diseases: While it is estimated that, for example, approx. 12.000 persons annually die from side effects of non-steroid antirheumatic drugs such as ASS and diclophenac (mostly due to stomach problems and internal bleeding) in the USA, and more than 1.000 in Germany (Jöckel 2002), no lethal complications have ever been observed from radon treatments. In addition, it is an advantage of radon therapy that it is inexpensively available in poorer parts of the world without affordable access to commercial pharmaceuticals for a large part of the population. Incidentally, the term "radon spa" may be somewhat confusing, because in some countries a "spa" is more associated with entertainment , "wellness", weight reduction, drug abuse correction, etc.. In a modern European radon spa, patients, with the treatment mostly paid for by the governmental health insurance, usually stay for about three weeks in clinics and receive the radon treatment under careful medical supervision as a prescription with careful control of the results. Nevertheless, the different and normally more healthy and relaxed environment, stimulation by a different climate, new social contacts, and other factors certainly contribute to a feeling of improved well-being. However, new randomized double-blind studies demonstrated distinctive long lasting additional positive radon health effect.

2. Therapeutic experiences before the discovery of radon.

Palaeolithic offerings found near The Gastein sources in Austria suggest that already in prehistoric times therapeutic radon effects may have been appreciated there. As far as known, the Italian island of Ischia in the volcanic area around Naples, settled by Greeks from Euböa about 2500 y ago, has been the first place in which warm radon sources have been used on a larger scale, and continue to be used for therapeutic reasons (Deetjen, 1997). Antique artificial grottoes and bathing tubs cut out of the rocks cannot be exactly dated, but have in common a high radon concentration of the water.

The first written documents on health effects observed in Ischia are by Gulio Jasolino in 1559 on "the natural therapy on the island Ischia", followed in 1835 by a book by J.E. Chevalley de Rivaz.. In 1917, M. Curie discovered high radioactivity in Lacco Ameno and identified it as radon.. The treatment is usually by inhalation or bathing, but also with sand which is also heated by emerging volcanic steam. Main indications for treatment are arthropathies (Sunta 1997). It is likely that the use of the famous old spas in the alpine regions of northern Italy such as Merano (2.000 Bq/L in spring water) and Lurisia (40.000 Bq/L) (S. Genchi and B. Colombo 1997) also date back more than two thousand years to ancient Roman times. Another example is Steben/Germany, with records of "strange properties" of a radon source from 1473, and the medical properties of this source described in 1690 (Skorpea 1990). In other cultures such as Japan, the radon effect (e.g. in Misasa) has also been a matter of empirical experience for many centuries.

There are numerous other locations now known as radon therapy facilities which have already been used as spas long before knowledge of ionizing radiation and radon. It was generally known since the Middle Ages that the miners in the silver miners of Saxony/Germany and nearby St. Joachimsthal in Bohemia (now Czech Republic), although working under very difficult and generally unhealthy conditions and frequently suffering (and dying early) from lung diseases (K. Becker 2003), had less problems with arthritic and similar diseases than the rest of the population. Therefore, the miners had sometimes uranium containing ore residues sewn into their clothes. They drank water which originated in the mines, and the local population used pitchblende (U ore) packages for the external treatment of inflammatory diseases (W. Schüttmann 1987). A C. Bruschius already wrote in 1548 in a description of the high-radon Fichtelgebirge/Germany: "Here people get very old, have few diseases, and recover quickly if they have any."

Known for many important medical discoveries such as the fundamental truth "It is the dose which makes a poison", the famous mediaeval physician Paracelsus devoted in 1525-1527 a chapter of a book on health sources to "bat Castein" (Bad Gastein/Austria - Windischbauer 1959), and in 1780 the "Thermis Gasteinensibus" (Gastein thermal bathes) were the subject of a dissertation. In 1553 and 15712, encyclopaedias about health spas were published (Van Tubergen and van der Linden 2002), and 1828 it was noticed that the electrical properties of the waters in Gastein were different from ordinary water. Half a century before the discovery of radioactivity, the famous German chemist Justus Liebig was advised by his physician to visit Gastein for treatment, but at first refused to go there because his chemical analysis of the local water showed no analytical evidence of being much different from his home tap water. After further medical advice, Liebig eventually underwent the treatment and found relief. He concluded that an unknown constituent, perhaps "something electric", was responsible for this effect.

Results published in 1864 also concluded that "electricity is the main reason for the effect of the sources on the organism" in Gastein (Sieveking 1907). Thus radon spas have been popular in quite different cultures and at times long before radon had been identified. It was also known for a long time that water from such sources, used long after having been bottled, did not have the healthy effects of "fresh" water, thus indicating the presence of a fairly rapidly decaying factor in the water. .

Even after it was first pointed out in England in 1903 and almost simultaneously in Germany in 1904, that radioactive gases are responsible for the therapeutic effects of such sources, more or less accidental "discoveries" of positive radon health effects continue up to recently in areas where little or nothing had been known about radon therapy. For example, some former uranium mines around Boulder/Mont./USA such a "Free Enterprise Radon Health Mine" started operation in the early 1950's. years. Some people even bring ageing cats and dogs for radon inhalation, and there were a book (Lewis 1994) and a few articles in

popular journals (Singer 2001, Bethell 2002). Other, earlier attempts to establish radon therapy centers in Canada and the USA, including "Lincoln Bath House" in Saratoga Springs/New York established in 1929, with the capacity to treat up to 4.500 people daily. There have also been "Radium Springs" in Arkansas, Virginia, New Mexico, Georgia, Oklahoma, and British Columbia, but little is about results of these spas (J. Muckerheide, pers. comm.) .

3. The first decades of scientific studies on radon sources and therapy.

The history of the radon discovery has been summarized before (Schüttmann 1988). The first publication about the radon in spa water (then called "radioactive emanation", following a suggestion by E. Rutherford in 1900) appeared in two reports about the thermal sources of Gastein/Austria in 1904 (Mache 1904a and Mache 1904b). Mache also introduced the first unit for radon activity concentrations, which was named after him (Mache-Einheit, ME) and mostly used in the German/Austrian literature, while the anglophonic countries preferred the "Curie" that had been introduced in 1910. One ME corresponds to 364 pCi/L. Other units have occasionally been used, e.g. the "Stat" (St), with 1 ME = 1 mSt/L, and the "Eman", with 1 ME equivalent to 3.64 Eman. Other unusual units also appeared, and rather quickly disappeared. In summary, 1 Ci corresponds to 37 GBq, 1Bq is 27 pCi, or 1 ME equivalent to13.5 Bq/L. Other units are the potential Alpha-Energy Concentration (PAEC) and the Working Level (WL), from which the Working-Level Month has been derived as a product of concentration and exposure time. It is nowadays mostly used for miner exposures (Rühe 1992), and concentrations are usually presented according to the SI system in Bq/L for water, and Bq/m³ for air. In this review, all values have been translated into Bq.

In 1906, a list of the radon content in more than 30 sources in 11 spas in Austria, Bohemia, Germany and Italy has been published (Sieveking 1906), with values up to 80.000 Bq/L in Gastein/Asuria, 70.000 Bq/L in Baden/Germany, and 182.000 Bq/L in Schlema/Germany (Hindenburgquelle) (Ebert and Keßler 1990). Currently, the Wettinerquelle in Brambach/Germany is considered the world's strongest, but there are also Japanese claims to this record. The information about the activity of sources sometimes varies substantially due to specific conditions and uncertainties in the measurements, fluctuations in the source strength, evaporation of radon as a function of interaction time with the atmosphere, exact location, atmospheric condition, and many other factors. In one booklet (Ebert 1999), for example, values measured in March/April 1913 are given as 54.000 Bq/L in Schlema/Germany in a source not available any more, 30.000 Bq/L in Brambach/Germany, 5.000 Bq/L on Ischia/Italy, and only 3.000 Bq/L in Gastein/Austria.

In some cases, high values have been claimed in order to make a spa more competitive. In Regarding radon concentrations in the air of caves, former mine shafts, and other underground facilities, claimed radon concentrations require careful investigation regarding the conditions and duration of the measurements. For example, in a "hospital cave" in Hungary, variations between < 1.000 Bq/m³ in winter and 22.000 Bq/m³ in

summer have been measured. In another cave (Pal Valley Cave), the radon level dropped from 2.500 Bq/m³ to essentially zero within three hours due to a cold weather front on Dec, 21, 1994 (Szerbin 1996 and 1997). Such pronounced fluctuations can to some degree be averaged by long term (3-12 months) integrating measurements by modern electronic or track etching detectors, but even then a reliability better than 20-30 % can hardly be expected, and all values expressed in three or even four digit numbers indicate a profound lack of understanding radon metrology.

It should be emphasized that the interest in radon therapy had little or no relation to the popular fashion between about 1910 and 1940, mostly in Europe, to attribute a multitude of healing powers to radium. There have not only been external sources such as Ra-impregnated bed blankets and compresses, but more importantly for Ra intake. For example, radium was added to many "health food" items such as crackers, tea, coffee, and chocolate. A German patent of 1931 (Senftner 1931/1936) describes how by adding radium bromide radioactive chocolate can be made. There are numerous publications describing such unconventional ways of health applications of Ra and as well as radon, e.g. in Ra-containing "emanators" for producing radon drinking water. Many of these activities may nowadays be considered just as historical footnotes, while there seems, in the light of modern research on beneficial low-dose effects, to be more than a grain of truth in others, as hormesis has to be considered a central issue in modern toxicology (Calabrese and Baldwin 2003).

Radon treatments can be carried out by inhalation from "natural" sources, e.g. in mine shafts or caves, or by bathing in Rn-containing water. Drinking radon water became less common in recent decades. Of course, radon can also be produced independently from the availability of natural sources by extracting it from radium or other sources - first proposals for the therapeutic use in 1903 in England actually suggested the inhalation of thorium emanation for the treatment of tuberculosis (Soddy 1903); in 1904. First results of such a treatment have been published (Sharp 1904). Radon uptake into the human body was studied in Germany (Elster and Geitel 1904). First radon treatments were carried out in Vienna (Neusser and Dautwitz 1905), including experiments with the external application of uranium ore material, or uranium-containing sand in bathtubs in order to produce radon-containing water. The first specific application for acute and chronic rheumatism of joints was reported in 1907 in Bohemia (Kraus 1907), and a physician in Braunschweig/Germany (Loewenthal 1906) studied, using radon water made from Ra compounds, whether "in small concentrations emanation causes any constant reactions in the health of the human body".

He treated patients for chronic joint rheumatism, and noticed that their reaction was very similar to those in spas. Further studies were summarized in two books by German scientists in 1912 and 1913 on radium therapy, biology, and research (Loewenthal 1912, Lazarus 1913). Many of these early studies were performed by bathing in water prepared by long-time submersion of cloth-wrapped uranium ore residues in special water barrels.. Several of the early investigators also looked for possible detrimental health effects,

but could not find any. First treatments with natural radon water (besides the traditional spas) at new locations selected for the high radon concentrations in the effluents of mines took place in St. Joachimsthal/Bohemia in 1906 with 43 patients. Almost all of them were treated for goat, chronic rheumatism, and neuralgic problems, and the results were described as “extremely successful” (Gottlieb 1907). In 1910 already 373, and 2.476 patients in 1913 came for treatment, and a Governmental Spa Institution opened its facilities in 1911. Between 1910 and 1912, the world-famous “Radium Palace Hotel” was built. It is still in operation with its facilities usually filled to capacity.

Around the same time, traditional spas with high radon concentration, such as Gastein/Austria and Baden-Baden/Germany, had started to offer specific radon treatments. Probably the first traditional spa that installed an overground radon inhalation facility “inhalatorium” was Bad (Aschoff 1912). It reopened in 1974 (Muth 1974). Treatment has also taken place in mine shafts since 1912, and overground inhalation facilities were established in France.

In Brambach/Germany, in 1910 the at this time strongest source was discovered (30.000 Bq/L).. A typical example for the increase of patients inthe new radon spas was the “Radiumbad Oberschlema”/Germany, also close to St. Joachimsthal, with a steady increase of patients from 300 in 1918 to 17.000 in 1943. In 1937, the Institute of Biophysics of the Kaiser-Wilhelm-Society in Frankfurt established a dependance especially for radon research in Schlema (Schüttmann and Aurand 1991). At the end of WW II, the activities in Schlema were abruptly stopped, because the area became one of the world` s largest uranium mining centers, supplying until 1989 about 240.000 t of uranium for the Soviet nuclear arms program. Only after the end of the Cold War, the Schlema Spa successfully reopened in 1998 (Schüttmann 1994, Ebert and Keßler 1998).

The history of radioactive springs in Japan, which is one of the countries with most hot springs in the world, dates back to 1909, and a review on the mineral springs of Japan was already published in 1915. Most of them are radon springs, but some are also high in thoron. Best known are the springs of Misasa with a radon level up to 3.000 Bq/L in the Gunze-no-yu source, but there are other sources in Masutomi, Ikeda, etc., in which much higher concentrations, one of them believed to be with up to 130.000 Bq/L to be the strongest in the world. Many studies on various aspects of radon therapy including pharmakokinetics, clinical experiences, etc. (most of them written or directed by Y. Oshima) were carried out in Japan (Morinaga 1958).

Further progress in the investigation of radon sources also proceeded in Europe, e.g. in the Nahe Valley/Germany (Wagner 1938). In other countries such as Israel, the radioactivity of sources was explored (Rosenblatt and Lindeman 1952). The search for new strong radon sources, and their possible use for establishing a radon spa, still continues. For example, the Fichtelgebirge in Northeastern Bavaria/Germany

is known for high radon concentrations in water and air (values exceeding 700.000 Bq/m³ have been measured in the air of a public water supply facility in the city of Hof in this area). The creation of a radon spa has been considered there (G. Bach et al. 1989) and in other parts of Europe. Several international organizations are involved in the study and promotion of radon balneology. The International Society for Medical Hydrology and Climatology (ISMH) is represented in 42 countries, with sections in Germany, France, Spain, Portugal, and Belgium (Pratzel 1994). This organization issued in 1995 Guidelines for Radon Balneology (Pratzel 1995), and an International Committee on Radon in Medicine (ICRM) exists within this society.

In the Association of German Radon Spa Physicians, about 14 German and Austrian radon spas treating approx. 75.000 patients annually are associated. A periodical is since 1994 almost completely devoted to radon balneology (Sansoni 1994). Furthermore, in 1991 a Radon Information and Documentation Center "RADIZ" has been established by K. Aurand (Curiestr. 3, D-08301 Schlema/Germany, Phone/Fax x493772-22926, e-mail RadizeV@t-inline.de <mailto:RadizeV@t-inline.de>), which maintains an archive of literature related to radon therapy and publishes brochures (about 20 so far) dealing with radon-related issues (Ebert 2001).

There are several recent books on radon therapy (e.g. Pratzel and Deetjen 1997), and numerous national and international conferences have been largely devoted to radon therapy. To mention only a few which took place more recently:

- Physical, Biological, and Medical Effects of Low-dose Ionizing Radiation, Bad Münster am Stein 1984 (Dirnagl 1984),
- Biological and Therapeutic Effects of Radon, Bad Hofgastein 1987 (Deetjen 1988),
- Physical, Biological and Therapeutic Effects of Low-dose Ionizing Radiation, Bad Münster am Stein 1989 (Deetjen 1990),
- 2nd Biophysical Workshop (Schlema 1991),
- Internat. Symp. of Techniques and Curative Treatment with Radon, Deneschi/Ukraina 1992 (Sansoni 1992),
- Benefits and Risks of Low Doses of Ionizing Radiation, Schlema/Germany, Oct.4-6, 1993 (Aurand et al, 1995),
- International Symposium Radon in Health Resort Medicine, Ischia/Italy, April 5-10, 1994
- Radon and Health, Gastein(Asutria 1998 (Deetjen and Falkenbach 1999)
- 3rd Biophysical Workshop on Medical and Biological Effects of Radon Balneology and Low Radiation exposures, Sept. 7-9, 2001 (Schlema 2002).

There have also been numerous international meetings in which the emphasis has been more on residential radon measurements under the aspect of possible lung cancer induction (e.g. Burkart et al. 2002, Peter et al. 2002, Sarenio Ed. 2002). The highly controversial issue of risk/cost/benefit assessment for residential

and industrial radon, and the very substantial literature on this subject (Becker 2003) is, however, not a topic of this review.

4. Radon therapy of degenerative diseases of joints and spine in Western Europe

Among the currently best known radon treatment centers with medical supervision are in

- Germany: Bad Brambach, Bad Kreuznach, Bad Münster am Stein, Schlema, Sibyllenbad, Bad Steben,
- Austria: Bad Gastein, Bad Hofgastein, Bad Zell,
- France: Plombieres,
- Italy: Ischia, Meran,
- Russia: Pyatigorsk, and
- Japan: Misasa.

In addition, there are numerous less known radon therapy centers, for example nine in Greece with radon concentrations up to 8.000 Bq/L in Ikaria (Kriditis et al. 1986), inhalation facilities in several health spas in France, as well as bathing sources in which radon is not the dominating component, but used in combination with minerals, SH2, and CO2.

Painful inflammatory or chronic rheumatic and arthritic diseases, such as rheumatoid arthritis, have historically been the first indications for radon treatment. They are among the most widespread health problems in humans even before middle age (see TIME cover article of June 9, 2003: “The coming epidemic of Arthritis”), and still remain the primary indication for radon therapy. There are also related illnesses, such as spondylitis ankylosans, a painful permanent bending if the spine known also as Morbus Bechterew. It occurs in around 0.1 to 5 % of the population, depending on geographic region. In Europe, the rate is around 0.2 %, and it already becomes evident between 16 and 40 y of age. Among the about 7.000 annual patients in Gastein/Austria, most are treated for this disease (Falkenbach 1996, Falkenbach and Wolter 1997, Falkenbach 2001). In a careful recent study, it has been found that the radon group showed a clear reduction in the pain and improvement of the spine flexibility up to nine months after the treatment (G. Lind-Albrecht 2002). Most of the current results of radon balneology have been published in German (e.g. Falkenbach et al. 1996), with only recently some articles also appearing in English (Franke et al. 2000, Falkenbach 2001). Of particular interest in the Morbus Bechterew therapy are studies about the combination of radon therapy and exercise treatment (Van Tubergen and Hidding 2002), which clearly show the superiority of the added radon treatment, with the longer lasting effect clearly compensating the higher cost of such a combination.

5. Current status of radon therapy and randomized double-blind studies

There still remained doubts about the effect of radon treatments in large parts of the medical and scientific

community, because it contradicted the widespread regulatory paradigm of lung-cancer inducing effects of the alpha radiation from radon down to very small doses. One of the problems in the quantification of pain-reducing effects is that there exists not yet a method for precisely measuring chronic pain. There are, however, well-established methods such as the application of a defined spot pressure (in kg/cm²) to established pain-sensitive "tender points" (Fig. 1) on a scale between zero and unbearable pain, and using this scale as a rather well reproducible cohorts. Complicating factors may be confounders, such as other constituents of the mineral waters, and the difficulty to carry out double-blind studies in underground inhalation facilities.

This situation changed after 1990 with randomized clinical prospective double-blind studies, with neither the patient nor the medical staff knowing about the identities of those in the control (placebo) and the radon groups, and with both groups treated under otherwise identical conditions. Such tests are generally considered as "the gold standard" in medicine for demonstrating therapeutic success. The pioneering work was done in the German radon spa Schlema in 1992, and repeated in Bad Steben in 1995, by Pratzel of Munich University (Pratzel 1992, 1994, and 1997, Pratzel et al. 1997). The results of these tests carried out as schematically described in Fig. 2, were rather unambiguous (Fig. 3 and 4). The radon concentrations in the bathes were 3.000 Bq/L in Schlema and 800 Bq/L in Bad Steben. In Schlema the patients also received other standardized treatments such as massages and gymnastics, but not in Bad Steben.

In natural sources the situation is frequently complicated by the presence of confounders such as minerals, SH2, and CO2, which also may have biopositive effects interacting with those of radon. There are several studies on this subject. For example, in Bad Brambach/Germany 30 patients each have been treated for rheumatoid arthritis with water containing both CO2 plus radon, and with CO2 only (Reiner 1998, Skorpea 1999). Using a combination of several indicators as a relieve parameter, there was no significant difference between the two groups at the end of the treatment, but a significantly longer lasting relieve for the radon group than the CO2 group three and six months after the treatment. In summary, the results of four randomized double-blind studies which were performed between 1993 and 1997 (Reiner 2002) are show in comparison with the control groups (Fig. 5), the bars indicating the 95 % confidence limits. Short term effects are given in the upper third, mid-term effects in the middle, and long-term effects in the lower part. The summary of all studies is given on the bottom line.

There also have been studies in which no positive radon effects could be demonstrated. For example, the indication "peripherical circulatory disturbances" cannot be derived from radon effects on skin blood flow (Knorr et al. 1990), and ergometric measurements of the heart frequency could not demonstrate relevant changes in the cardio-pulmonary system (Leiner and Aigner 1984).

6. Radon therapy in the former Soviet Union

This topic, overlapping with and supplementing the progress in Western Europe, deserves special attention because of the volume of research as well as the number of applications. For example, around 1984 about ten million (!) radon applications were delivered to one million patients annually in spas, sanatoriums, and in outpatient departments of the USSR health system (W. M. Bogolyubov et al. 1984). The reasons which made it one of the most popular types of balneology among patients as well as physicians were the easy accessibility, safety, efficiency, and low cost of such treatments. It was carried out mostly with "artificial" radon obtained from a wide network of radium sources from which the radon gas was locally extracted. Also in other countries such as Germany, radon emanation equipment for drinking or bathing at home was still available in the 1950s. (Aures 2003).

There are at least one thousand publications in Russian journals and conference proceedings on this subject, among them ca. by S. A. Andreev of All Union Research Center for Medical Rehabilitation and Physical Therapy in Moscow and his colleagues. Another center of radon therapy and research was Pjatigorsk in the Caucasus Mountains with sources of 2.700 Bq/L. About one hundred of the more important papers became available in German translations, which, together with some reviews (B. Legler 1994), are the basis of the this brief summary.

First investigations about radioactivity in Russian spas date back to 1902-1903. Therapeutic concentrations of radon in mineral waters were found 1911 in Pyatigorsk and Tshaltubo. Between 1909 and 1914, well-equipped radiological laboratories in Omsk, Odessa, Moscow and St. Petersburg have been established, and carried out investigations on radon therapy. In 1920 (after interruptions by WW I, revolution and civil war), a State Institute for Balneology was founded in Pyatigorsk. Around 1922-23, in Petrograd (St. Petersburg) the first strong (1 g) radium sources has been used for distribution of radon to other treatment facilities. Careful studies on the preparation of radon sources, radon dosimetry, absorption properties, uptake through the skin, pharmakinetics, etc., followed during the next decades. In particular, because radon concentrations and other parameters including temperature, added CO2 and other gases, could easily be varied with the "artificial" radon sources, and with the compliance of the study groups being excellent, many systematic investigations in this area have been performed. During 1955-1960, hundreds of radon laboratories were established for the daily production of radon for therapeutic use.

After 1960, investigations centred on radiation protection issues related to radon therapy (organ doses, etc., Andreev 1973), radiobiology, new therapeutic equipment, pharmakinetics of radon in the body (Andreev 1971), radon penetration through the skin (Andreev 1989), comparisons with placebo groups, etc. This also led to the demonstration of radiation hormesis (Andreev and Selenezkaya 1998). To quote from a summary report: "The received data irrefutably showed the presence of therapeutic effects of small doses of ionizing radiation (hormetic curves in clinics) which cannot only be revealed, but assessed numerically by properly organized research."

During this period, the daily number of radon applications with improved equipment (Gussarov et al. 1980), under medical control, and according to governmental radiation protection regulations, increased up to 5.000 for each of the many radon treatment facilities (Gusarov and Andreev 1972). Later, with the risks associated with very high radon doses becoming better known, risk/benefit assessments of radon treatments were studied in more detail (Gussarov and Andreev 1983, Bogoljobov and Andreev 1985). There was limited access to international literature, and contacts to Western scientists (during WW II and the Stalinist post-war period, contacts with Western European scientists and references to their work were prohibited. Not much is known about the current status of radon balneology in the former SU states, but it could also have suffered from the breakdown of social structures and governmental health services in the post-Soviet area.

There were many types of radon application there, including full or partial bathes in bathtubs and swimming pools, with and without other balneological components being added; partial or full-body air exposures, with or without air circulation (for two typical devices, Fig. 6 after Bogoljubow 1990); inhalation (with or without decay products); irrigation of nose, mouth, rectum, vagina; and local applications (ointments, packages, etc.). The spectrum of indications which has been tried more or (often less) successfully is also very wide, including

- heart and circular problems (hypertonia, etc.),
- blood circulation (artherosclerosis, thrombophlebitis),
- pulmonary problems (bronchial asthma, chronic bronchitis),
- inflammatory or degenerative diseases of the skeleton (which is in Western Europe nowadays the primary indication),
- diseases of the nervous system (e.g. neurosis),
- chronic inflammations, sterility and climacteric problems in gynaecology,
- skin diseases (psoriasis, neurodermitis, chronic eczema), and
- gastrites, ulcus ventriculi. .

The best results were obtained with rheumatic diseases, in gynaecology, skin diseases and hypertension.

The contraindications in the SU clinics have been similar to those in Western Europe: Acute infections, psychic diseases, pregnancy, tumors, active tuberculosis, epilepsy, acute serious diseases of internal organs, infected open wounds, and haematological irregularities. Alcohol was also forbidden during the treatment, and a classification of radon concentrations in water used for treatments has been used, with low concentrations up to 500 Bq/L, medium concentrations up to 3.000 Bq/L, and higher concentrations above this level. Among the many interesting results of the Russian studies, those about the relation between radon concentration and desirable health effect (Fig. 7)are of particular interest (Davidova 1984, Andreev 1990). Obviously, the dose-effect relation in patients with recidivous rheumatism (in the state of minimal

process activity, using 15 bathes of 10 min. each) shows a clear maximum in the improvement of the patients around 3.000 Bq/m³, corresponding to a skin dose of about 2 mSv.

In another study (Strelkova et al.1980), various rheumatic diseases have been investigated, in for instance with groups of 148 patients each with cervical pain syndrome. In the response to 12 bathes at different radon concentrations, in comparison with the control group with ordinary water, 25 % showed improvement with normal water, 40 % at 500 Bq/L, and 55 % at 5.000 Bq/L. However, undesirable side effects were observed above 2.500 Bq/L. Further summaries of the substantial Russian activities in radon balneology are scattered in the literature (Tauchert 1972, Bogoljukov and Andreev 1994, and Davydova 1994).

6. Mechanism and pharmakokinetics of radon effects.

There are at least three reasons why the positive effects of low radiation exposures have not yet been fully explained:

- Experiments on the molecular or cellular level are difficult to extrapolate to the effects on the whole organism, which involves complex compensation and repair mechanisms such as apoptosis, adaptive response, bystander effects, and positive stress stimulation.
- Epidemiological studies frequently fail in the low-dose range because of serious confounders, such as smoking in the case of lung cancer, or too large populations required to obtain conclusive results.
- In the current structure of public and governmental support for radiation effects research, emphasis is on detrimental health effects, with biopositive (therapeutic) aspects frequently being ignored as disturbing for the official paradigms, governmental regulations, and official anti-radon campaigns.

This general situation explains to some extent why the experimental animal and human studies regarding the mechanism of biopositive radon effects has, despite intense research in many countries, not yet been able to completely clarify the mechanism of therapeutical radon effects. There is a long history of metabolic and radon effect studies which is impossible to cover in a brief review. As an example, a study about the effect of radioactive thermal water on the inactivation of noradrenalin (Wense 1955) may be mentioned, or “the stimulation of natural killer cells, anti-oxidant compounds, and DNA repair enzymes, and a decrease in C-reactive protein” (Van Tubergen and Hidding 2002).

According to Russian research (Andreev et al. 1990), the radon in bathing water penetrates the skin and forms a depot accumulating up to 60 % of the radon uptake, and reaching 20-30 % of the radon concentration in the water. The radon is then absorbed in the fatty tissues, and the radon daughter products are accumulated in the kidneys. The organ doses for a 15 min. bath at 1.500 Bq/L has been calculated at 0.1 mSv for the skin, 0.003 mSv for the kidney, and 0.0015 mSv for body fat. Two hours after bathing, only 10

% of the original radon intake still remained in the body. Short-lived radon daughters contribute about 70 % to the absorbed dose. Diffusion of free radicals produced in the skin may contribute to the effect by affecting skin receptors and regulatory mechanisms.

Recently, the more general explanations such as stimulation of the immune system (Soto 1997) have been replaced by more detailed studies including the influence on Langerhans cells, increase in the encephaline level, reduction of oxygen radicals in the neutrophiles and macrophages, influences on homoeostasis, factors influencing the attachment of leukocytes at joint tissues, etc. For example, in a series of animal (rat) experiments by a Japanese group (Ma et al. 1996), the effect of inhaled radon on the activity of an important enzyme, superoxide dismutase (SOD) in different tissues has been investigated as a function of the radon concentration, showing substantial stimulating effects in liver and kidney. In summary, unlike the essentially pain-relieving non-steroid drugs, the radon effect is by most experts nowadays considered primarily based on a stimulation of the defensive immune system, and therefore to be classified as not only evidence-based, but at least partially explainable modern medicine on the cellular and whole-body levels.

There are recent studies on the surprisingly long-lasting radon progeny activity on skin and hair after exposure to the humid warm air in the Gastein mine shaft (Falkenbach et al. 2002). Due to these high adhesive properties, the period of exposure of the Langerhans cells is extended, with perhaps systemic effects mediated by their alteration. On the other hand, as demonstrated in measurements of radon exhalation rates in persons submersed in radon water and other investigations such as the transfer of unattached radon daughter products from the pulmonary tract to the blood of humans (Butterweck et al. 2002), the half-life of radon in the body has repeatedly been confirmed to be the order of only 20-60 min. to a few hours, depending somewhat of the aerosol size distribution in case of inhalation. Radon accumulates primarily in fatty tissues. In one of those studies, the transfer of radon through the skin to the lungs and exhalation has been examined in humans, resulting in an almost complete exhalation 50 min. after the commencement of a 24 min. bath (Grunewald and Grunewald 1995).

Already in 1911, an increased excretion of purin bases and uric acid in urine was observed as a result of radon treatments, which was a positive aspect for the treatment of gout, but also seemed to indicate a destruction of nucleoproteids (Meseritzky 1911). It was recommended to restrict the radon concentration in drinking treatments to 14.000 Bq/L. In the same year, it was reported that the oral application of radon leads to a fast transfer to placenta, foetus, and mother’s milk (Lazarus 1911). Those studies (Schraub 1958) indicate an early interest in potential radon health risks. On the other hand, it was shown that fractionated alpha radiation (2-4 h/d), in addition to the normal environmental exposure, did not increase, but decreased the number of chromosome aberrations due to a stimulation of repair mechanisms (Pohl-Rüling et al. 1979).

8. Dose Levels, Administrative Questions, and Outlook.

The annual effective dose equivalent to patients (assuming one sequence of radon treatments) is usually in the order of 0.1 to 3 mSv and thus within the normal fluctuations of natural background exposure levels. However, the treatment personnel (doctors, nurses, drivers of patient trains) may receive up to approx. 100 mSv according to one study (Kritidis et al. 1986). In other investigations (Andreev 1995), the skin dose amounted to less than 1-3 mSv for a series of applications in bathes, 1 mSv lung dose by inhalation, and < 0.1 mSv for the stomach for drinking radon water. Other authors (e.g. Tempfer et al. 2003) confirm these values. Nevertheless, one of the problems for the more widespread use of radon therapy are governmental radiation protection regulations, which are based on the ICRP/IAEA/NCRP/EU assumption of the hazards associated with radon. It was well established in recent years that there is a threshold around 600 to 1.000 Bq/m^3 in air for the permanent intake, in particular at home and at the working place in areas of high natural U/Ra geological situations, for the lung cancer induction by radon in humans. However, essentially all observed effects essentially can be attributed to cigarette consumption (see recent reviews, based on investigations by Conrady, Martin et al.: Becker 2001, Becker 2002, and Becker 2003).

Nevertheless, the new "radon protection" regulations to be legally enforced in several countries make it difficult or impossible to establish new radon treatment facilities there. In others (such as Austria, Czechia, and Germany) with a long tradition in this field, radon therapy with natural water or air sources is at least tolerated by the authorities, as long as the personnel working there is supervised by personnel monitoring devices according to the regulations for "radiation workers", using passive track etching polymer track etching detectors, or new electronic systems. The practice of producing "artificial" radon by extracting the gas from radium sources seems not to be legal any more. (Ulrich 1994).

Among some other problems in the more widespread application of radon balneology are:

1. The radiophobic syndrome caused by anti-nuclear political and media campaigns scaring many potential patients.
2. National health insurance systems, with increasing financial problems due to the demographic and economic situation in Western Europe, are in the process of reducing their services by excluding from their coverage "natural treatments" such as mineral and radon spas.
3. Governmental organizations split between those responsible for radiation protection, and others in charge of public health. While the first promote the public "dangers" due to even low residential and professional radon exposures (Schüttmann 1997, Becker 2003), the health authorities are becoming reluctant to promote research in areas which some public health administrators still consider not part of evidence-based medicine..
4. Last but probably not least, the influential lobby of the pharmaceutical industry is more interested in promoting the profitable large-scale use of non-steroid antirheumatic drugs, and succeeded to

convince most of the medical community of this form of therapy instead of exploring the drug-free and relatively inexpensive radon treatments.

In conclusion: Radon, which is the largest contributor to natural population exposures, has been declared by several international and national radiation advisory bodies and regulators to be a powerful carcinogen causing, for example, 37.000 lung cancer deaths p.a. in Germany. At the same time, it has been successfully used as an effective evidence-based therapy against rheumatic and arthritic degenerative diseases for many centuries even without being known, and even more so after its discovery about one century ago. It is well known that the same physical or chemical agent may, depending on dose and other factors, have detrimental as well as beneficial health effects. Obviously, hormetic effects of stressants including ionizing radiation are more the rule than the exception in all areas of pharmacology, toxicology, etc., as well as for radiation effects (Hendriksen and Maillee 2003, Calabrese and Baldwin 2003).

Regarding radon therapy, it could for precautionary reasons be assumed that there may indeed be some negative effect at very high radon levels, and on particularly sensitive persons such as children and pregnant women, which may thus be excluded from treatment. On the other hand, the beneficial effects on people with painful degenerative joint and spine problems far outweigh such minimal, and to a large degree hypothetical, potential risks, and should not prevent the therapeutic application of radon under medical control, for the benefits of the patients as well as from a cost reduction point of view (Van Tubergen et al. 2001 - Fig. 8).

There is also increasing evidence of hormetic effects on the occurrence not only of lung cancer at above-average residential radon rates (Conrady et al. 2002), but also on other types of unpleasant health effects such as the occurrence of birth defects (Leichsenring 2002). Therapeutic radon uses appear to deserve further investigation, and could promote the understanding of beneficial radiation health effect in the low to medium dose range in gereneral.

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(*Remarks*: It was impossible to comprehensively analyze all publications on this subject. Many of them, in particular historical and Russian publications, are not accessible electronically and/or ISBN/ISSN. Also, the multitude of media reports, newspaper articles and other less reliable sources have not been quoted, but several earlier reviews are included up to early 2003, contaioning a large number of additional references. The reader may also consult “Radon balneology” under PubMed www.ncbi.nlm.nih.gov <http://www.ncbi.nlm.nih.gov>.

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Figure captions:

Fig. 1. Tender points used for testing the pressure sensitivity of patients with painful degenerative joint diseases by applying a variable pressure (Baumann 2002)

Fig. 2. Schematic diagram of bar-code regulated double-blind bathing studies in radon water (verum), and otherwise identical warm non-radon water (Kontrolle) (Pratzel et al. 1993)

Fig. 3. Tender point response of pain threshold with cervical spondylosis patients during a three week treatment, and (the two points at the right) 2 and 4 months after end of treatment, using radon and placebo tab water (Pratzel et al. 1997)

Fig. 4. A complex “painless parameter” comparing in a study the radon (black bars) with the control groups (light bars) at the end of the three-week treatment (left), and after 3 (middle), and 6 months after the treatment (Reiner 2002).

Fig. 5. Summary of the pain-reducing effects found in four randomized clinical double-blind studies between 1993 and 1997, showing in comparison with the control groups (bars indicating the 95 % confidence limits) the short-term effect (upper third), the mid-term (middle third), and the long-term radon effects. The summary of all studies is given in the bottom line (Reiner 2002).

Fig. 6. Boxes used in Russia for application (and research) of radon gas treatment including inhalation (left), and for exposure of the body skin only (right), including (left) the radon gas production (3), air heating devices (10 left, 7 right), radon control chamber (left 4), etc.

Fig. 7. Dose-effect relation in patients with recidiv. rheumatism in the state of minimal activity during treatment with 15 times 10 min. radon bathes. Ordinate: Improvement in each group as a summary of different parameters; abscissa: Radon concentration in kBq/L in the water and skin dose (in mSv) during total treatment (Andreev et al. 1990).

Fig. 8. Pooled index of change as a function of time (in weeks) in three patient groups for Morbus Bechterew treatment: Controls at home; group 2 with exercise treatment only; and group 1 (upper curve) for exercise plus radon treatment (Van Tubergen et al. 2001)