

Raymond Vahan Damadian(1936-)是美国医生,医疗从业人员,也是第一台MR扫描仪的发明者。Damadian对活细胞中钠和何的研究使他首次进行了核磁共振实验,使他首次在1969年提出了MR人体扫描仪

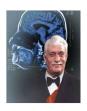
Dr Raymond Damadian, Pioneer of MRI





Dr Damadian with the history-making prototype of his MRI scanner. The first MR image of a human skull was made with this scanner on July 3, 1977. The prototype is now on permanent display at the Smithsonian Institution's Hall of Medical Sciences.

Assistant Larry Minkoff in Indomitable



'super-scientist' Dr Raymond V. Damadian



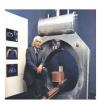


Damadian's cancer detector. Artist's rendering published in the New York Times on 9 February 1974.

Building the First MRI







Dr. Damadian with the history-making prototype of Dr. Damadian's MRI scanner. The first MR image of a human chest was made with this scanner on July 3, 1977 which he called the 'Indomitable'.

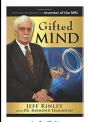
FONAR introduced the world's first commercial MRI in 1980, and went public in 1981

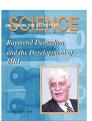
Dr. Raymond Damadian had plagiarized earlier work of Dr. Erik Odeblad

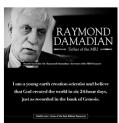


American doctor and scientist Raymond Damadian built a partial body MRI scanner in 1977, which he called the 'Indomitable'.

Gifted Mind: The Dr. Raymond Damadian Story, Inventor of the MRI







天才思维

Damadian, R. Tumor Detection by Nuclear Magnetic Resonance. Science, 1971, 171:1151-1153.

Creation scientist创世论科学家

Nobel Prize Controversies

The long-running and hostile dispute over who should receive credit for the invention of clinical MRI resurfaced during Sunday's Honorary Lecture at ECR 2014





Dr. Morton Meyers from East Setauket, New York. U.S.

According to Dr. Morton Meyers, a radiologist and historian from East Setauket, New York, U.S., there should have been a third recipient of the award: Dr. Raymond Damadian, founder of Fonar.

Nobel Prize Controversies

MRI is an "old" technique

Bitter conflict over recognition for discovery of MRI resurfaces in dramatic plenary session



Who develops and nurtures it to bring to everybody's benefit?

Nobel Prize Controversies



"You should get your facts and then talk," he said. Rinck added that Damadian had plagiarized earlier work by Dr. Erik Odeblad from Stockholm who should have received a Nobel Prize for MRI, because in 1955 he published the first medical NMR studies, including relaxation time measurements, of living cells and excised

Dr. Peter Rinck, PhD, chairman of the European Magnetic Resonance Forum and president of the Council of the Round Table Foundation

Erik Odeblad-The Forgotten Pioneer in MRI



2012年, Erik Odeblad荣获欧洲磁 共振奖时,展示了他 的第一台NMR谱仪

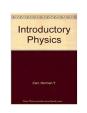
Erik Odeblad

1954年12月由Erik Odeblad 和Gunnar Lindström提交到Stockholm的Acta Radiologica杂 志并于1955年获得发表"生物样品质子磁共振的

MRI Pioneer- Herman Y. Carr



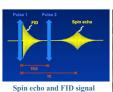




Herman Y. Carr (1924 -2008) was an American physicist and pioneer of magnetic resonance imaging. He received his Master's degree in 1949 and his Ph.D. in 1953 from Harvard University. His doctoral thesis, published in 1952, described techniques for using gradients in magnetic fields and was the first example of magnetic resonance imaging or MRI.

Erwin Louis Hahn (1921-2016)

初步观察结果"







"The person who really missed out the Nobel Prize for his contribution to the principles of Spin Echoes' in 1950, which are essential to modern day MRI.



What are the developments which lead to the MRI?

No single person or team invented the MRI in isolation; it is the culmination of decades of scientific progress and understanding. MRI technology begins with the discovery of a quantum-physics phenomenon called nuclear magnetic resonance (NMR) in 1937 by Isidor I. Rabi, a Polish-born American physicist.

NMR Vs NMRI Vs MRI





MR Image

Making an Image

Functional Imagina

Because of patients' worrying dangers of nuclearradioactivity, the word "nuclear" had been largely dropped in the mid 1980s when referring to Magnetic resonance (MR) imaging.

MR Vs NMR Vs MRI

Nuclear induction 核感应

Nuclear paramagnetic resonance 核顺磁共振

Nuclear magnetic resonance (NMR) 核磁共振

Magnetic resonance (MR) imaging (MRI) 磁共振成像

Nuclear Magnetic resonance imaging (MRI) 核磁共振成像

Magnetic resonance angiography (MRA 磁共振血流成像)

functional Magnetic resonance imaging (fMRI) 功能磁共振成像

MRI按主磁场的场强分类



1 T = 10000 G

-MRI图像信噪比与主磁场场强成正比

-低场: 小于0.5T

4.7 T=200 MHz 7 T=400 MHz 质子共振频率

-中场: 0.5T-1.0T

-高场: 1.0T-2.0T (1.0T、1.5T、2.0T)

-超高场强: 大于2.0 T (3.0T、4.7T、7T)

高斯 (Gauss, G)



地球磁场(the earth magnetic field)多强?

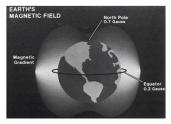
Carolus Fridericus Gauss (1777-1855)

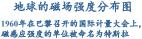
德国著名数学家、物理学家,于1832年首次测量了地球的磁场 1高斯为距离5安培电流的直导线1厘米处检测到的磁场强度



特斯拉(Tesla, T)"电气时代之父"

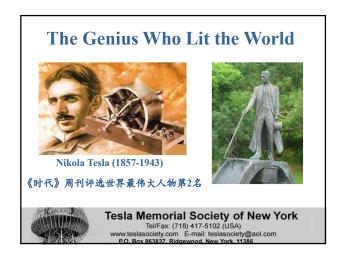
磁密度单位 (1Tesla=10000Gause)







Nikola Tesla (1857-1943) 奥地利电器工程师,物理 学家,旋转磁场原理及其 应用的先驱者之一。



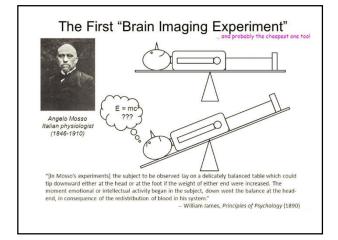


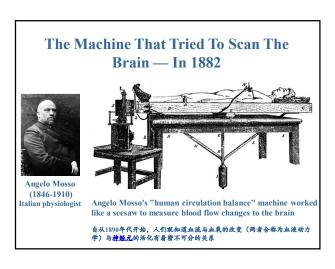
MRI Is A Unique Biomedical Imaging Technique

- MRI forms images from an intrinsic tissue signal that does not result from radioactive decay
- Computed Tomography (CT) and conventional radiography form images by measuring the attenuation of external Xrays

The MRI "Experience"

- Imaging is a slow process during which the subject must not move
- The magnet space is small and many subjects are claustrophobic
- The gradient hardware makes a very large amount of audio noise
- MRI is widely regarded as a safe biomedical imaging procedure
- - No (ionizing) radiation is used
- - No radioactive materials are used









Seiji Ogawa (小川 誠二) the father of modern functional brain imaging

The primary form of fMRI uses the bloodoxygen-level dependent (BOLD) contrast, discovered by Seiji Ogawa in 1990.



PNAS. 1992, 89 (13): 5675-79



Cover of November 1991 Science with an artist's rendition of the landmark paper by J. Belliveau

fMRI -1990: Ogawa observes BOLD effect with T2* blood vessels became more visible as blood oxygen decreased -1991: Belliveau observes first functional images using a contrast agent -1992: Ogawa et al. and Kwong et al. publish first functional images using BOLD signal



Seiji Ogawa 小川 裁二

Use in my office and the second process of t

Proc. Natl. Acad. Sci. USA Vol. 89, pp. 5675-5679, June 1992 Neurobiology

Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation

KENNETH K. KWONG¹, JOHN W. BELLIVEAU¹, DAVID A. CHERLER¹, INNA E. GOLDBERG¹, ROBERT M. WEISSGOFF, BROGTTE P. PORCELET, DAVID N. KENNEDY¹, BERNICE E. HOPPEL¹, AMAR S. COHLIN, ROBERT TURNER¹, HOMO-MING GENERO, THOMAS J. BADAY¹, AND BELICE R. ROSEN¹
**MICH.NET CHERC CHERC THE RESIDENCY AND SELECT R. ROSEN¹
**MICH.NET CHERC CHERC CHERC THE RESIDENCY CHERCAGE AND THE ADMITTANT CHERCAGE TO SELECT RESIDENCY CONTRIBUTION.

PMRI A NEWNIES

Jack Belliveau: The New Mind Reader



John (Jack) Belliveau 1959-2014



Dr. Belliveau had recently developed a technique to track blood flow in the brain, which he called dynamic susceptibility contrast, using an MRI machine.

Jack Belliveau was a scientist who shed new light on the thought processes of the human brain



John (Jack) Belliveau 1959-2014

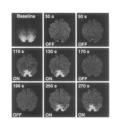


Belliveau also pioneered multimodal imaging, exploring the workings of the brain with combinations of fMRI and other imaging techniques

The Pioneer in Functional MRI



邝健民 Kenneth Kin Man Kwong Harvard Medical School



PNAS. 19992, 89 (12): 5951-5955

Most researchers credit Kwong and Ogawa independently with the discovery of what is now called Functional MRI (fMRI).

fMRI "Mind Reader"? Are you lying? Detector Library Detector



fMRI 读心技术-未来是否可以成为法庭上的证据? fMRI: Still Not a Mind Reader







Scientists Can Now Read Your Thoughts With a Brain Scan 大脑活动的可视化

历史上中毒事件

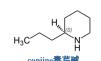


The Death of Socrates 苏格拉底之死

"Devil's Bread 魔鬼的面包"

"Devil's Porridge 魔鬼的粥"



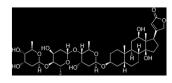




The Death of Socrates苏格拉底

"Angel of Death"- Digoxin





Charles Edmund Cullen (1960-) is an American serial killer. Cullen confessed to authorities that he killed up to forty patients during the course of his sixteen-year career as a nurse in New Jersey. Experts have estimated that Cullen may ultimately be responsible for 400 deaths, which would make him the most prolific serial killer in recorded history. He is currently serving a sentence of life in prison without parole for over 100 years, to be served consecutively with his other sentences in Pennsylvania.

马钱子碱Strychnine中毒



Agatha Christie (1890~1976) 英国女侦探小说家、剧作家,三 大推理文学宗师之一: 《东方快 车谋杀案》和《尼罗河谋杀案》







Halil Turgut Özal (Turkish, 1927-1993) was the 8th President of Turkey from 1989-1993

塑造历史的谋杀案

-简•斯坦福的死亡奇案



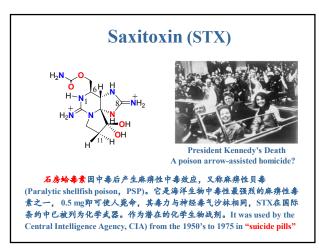
Jane Elizabeth Lathrop Stanford (1828 –1905) She funded and operated the university almost single-handedly until her mysterious death in 1905

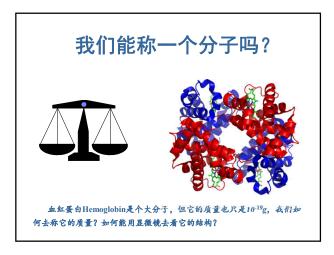


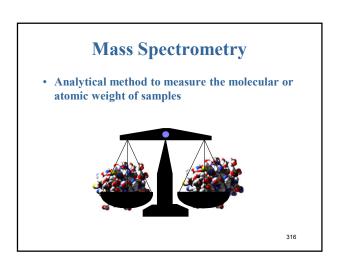


David Starr Jordan (1851-1931) The founding president of Stanford University

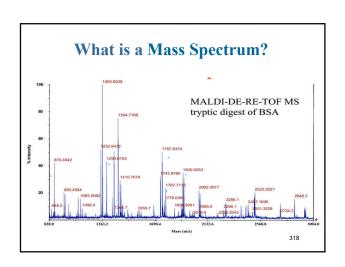












Application of Mass Spectrometry

- Biotechnology: the analysis of proteins, peptides, oligonucleotides
- Pharmaceutical: drug discovery, combinatorial chemistry, pharmacokinetics, drug metabolism, drug degradation product analysis
- Clinical: Therapeutic drug monitoring, neonatal screening, haemoglobin analysis, drug testing
- Environmental: Pesticides on foods, water quality, food contamination
- Forensic: Toxicology, identification of drugs

质谱发展史

1898 W. Wien 发现带正电荷的离子束在磁场中发生偏转。

1911 J. J. Thomson 使用简单的电场-磁场组合装置,获得了抛物纸族的质谱,证明了²⁰Ne,²²Ne两种同位素的存在。1906年诺贝尔物理学奖。

1918 Francis William Aston制得了第一台速度聚焦质谱仪。他获得了 1922年诺贝尔化学奖。提出每种同位素的质子和中子在結合成原子核时, 具有特定的质量亏损(并非整数值)。1922年诺贝尔化学奖。







Joseph John Thomson (1856-1940) 1906 NP

F. W. AST0320 (1887-1945) 1922 NI

The man behind the mass spectrograph



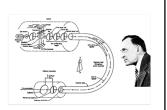


Francis William Aston熱爱运动,定期到瑞士、挪威等地参加超野滑雪、滑雪等冬季项目;花了相当多业余时间投入到自行车运动中。他还参与游泳、高尔夫/优英是在剑桥与卢瑟福等同事一起)、网球等运动,并且在英格兰、威尔士和爱尔兰举行的一些公开赛中获奖。1909年,他到檀香山学习冲液。出身于音乐世家的他,能够弹奏钢琴、小提琴和大提琴,时常在剑桥演出。另外,他还热衷于在世界各地旅行。

质谱发展史

1918 A. J. Dempster 采用电子轰击技术使分子离子化。





1945年Arthur J. Dempster 设计的质谱分析仪

322

质谱发展史

1981年英国曼彻斯特大学(1934-1991)开发了快原子轰击 电离(Fast-atom-bombardment Mass Spectrometry, FAB-MS) 应用,较好地解决了易分解的化合物的质谱测定。



Michael Barber

323

质谱发展史



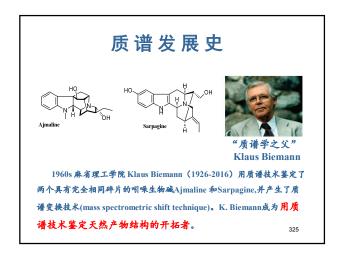




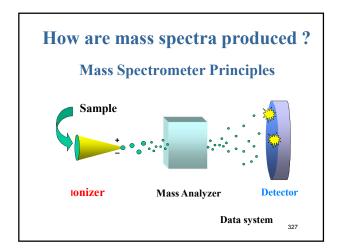
Wolfgang Paul (1913-1993) 1989 NI

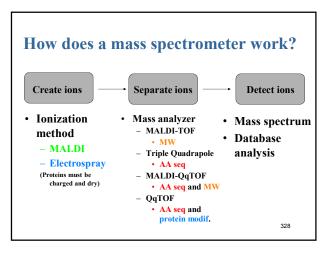
They co-developed the non-magnetic quadrupole mass filter which laid the foundation for what is now called an ion trap.

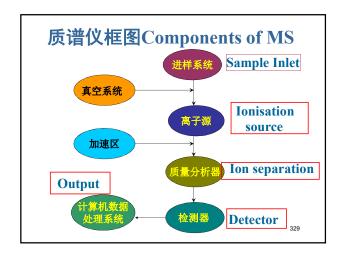
100多年的质谱史,已有11个诺贝尔奖授予了与质谱技术的诞生和发展以及有关应用方面的研究。











质 谱 Mass Spectroscopy ◆ 确定分子量 MW (Low Resolution) ◆ 确定分子式 MF (High Resolution) ◆ 了解分子内原子连接的详细情况 Unsaturation Number (UN) Hydrogen Deficiency Index (HDI)

如何测定生物大分子?如何离子化?

Weighing Proteins

A mass spectrometer creates charged particles (ions) from molecules. Common way is to add or take away an ions:

 $NaCl + e^- \rightarrow NaCl^-$

 $NaCl \rightarrow NaCl^+ + e^-$

It then analyzes those ions to provide information about the molecular weight of the compound and its chemical structure.

331

Mass Spectroscopy



2002年诺贝尔化学奖



田中耕一

2002年,美国科学家约翰·芬恩(John Bennett Fenn, 1917-2010)和日本科学家田中耕一 (1959-)因为发明了对生物大分子的质谱分析法获得了诺贝尔化学奖, 芬恩对成团的生物大分子施加强电场, 田中则用激光轰击成团的生物大分子。这两种方法都成功地使生物大分子相互完整地分离, 同时也被电离。它们的发明奠定了科学家对生物大分子进行进一步分析的基础。

332

基质辅助激光解吸/电离作用

诺贝尔化学奖引争议



田中耕一 1988年6月7日刊登 《质谱学快讯》

1988年7月5日刊登 但投稿提前1个月 《分析化学》

德国科学家Franz Hillenkamp (1936-2014) 和Michael Karas (1952-) 较田中晚两个月发表了基质辅助激光解吸/电离作用(matrix-assisted laser

desorption ionization, MALDI),更实用且两人在其后多年一直贡献良多。

Ioniizattiion Metthods

Electron impact (EI)

Chemical Ionisation (CI)

Fast atom bombardment (FAB)

Field desorption (FD)

Atmospheric Pressure Chemical Ionisation (APCI)

ESI Electro-Spray Ionization

MALDI Matrix Assisted Laser Desorption Ionization EI

334

Organic Mass Spectroscopy

优点:

- 1. 分析范围广(气体、液体、固体)
- 2. 测定分子量,确定分子式
- 3. 分析速度快,灵敏度高
- 4. 各种联用技术 (GC-MS, LC-MS, HPLC-MS)
- 5. 新的电离、检测技术 (EI, FAB, FD)

335

特点:

- ◆质谱不属波谱范围。
- ◆质谱与电磁波的波长和分子内某种物理量的改变无关。
- ◆分析范围宽,可对气体、液体、固体等进行分析。
- ◆质谱是分子离子及碎片离子的质量与其相对丰度的谱, **谱图与分子结构有关。**
- ◆质谱法进样量少, 灵敏度高, 分析速度快。
- ◆ 质谱是唯一可以给出分子量,确定分子式的方法,而 分子式的确定对化合物的结构鉴定是至关重要的。特 别是对于判断是否含有杂原子,判断化合物环的个数。
- ◆质谱仪器较为精密,价格较贵,工作环境要求较高,操作技术要求比较高,给普及带来一定的限制。
- ◆质谱破坏样品。

336

Mass Spectrometer



337

分子量、分子式的确定

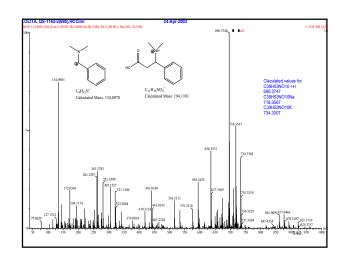
- Molecular ion ---- the m/z value of the molecular ion gives the molecular weight of the compound
- Base peak ---- is the one with the greatest intensity. (it is assigned a relative intensity of 100%)
- M+1 peak or M+2 peak ---- often occurs because there are naturally isotopes of carbon, or other atoms

If HRMS showed have an oxygen and The IR data revealed the absence of absorptions for hydroxyl group or unsaturation, suggesting that the oxygen is involved in ether linkages.

338

- High-Resolution Mass Spectrometry can determine the exact molecular mass of a fragment with a precision of 0.0001 amu.
- e. g. Some compounds with a nominal molecular mass of 122 amu and their exact molecular masses

339



计算不饱和度 Unsaturation Index

(Double Bond Equivalent, Indices of Hydrogen Deficiency)

不饱和单位(或称不饱和度,以Q表示)表示分子中存在 的双键或环的数目,是解析化合物结构的一个重要参数。 计算不饱和单位的方法如下:

$$\Omega = n+1 = \frac{H}{2} = \frac{CI}{2} + \frac{N}{2}$$

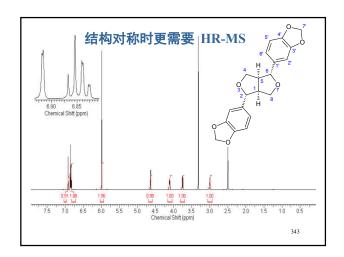
式中n为碳原子数目, Cl代表卤素, N是三价氮

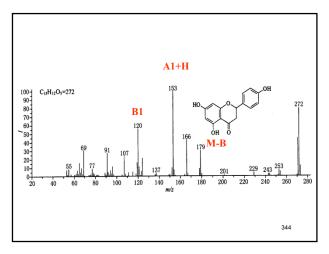
341

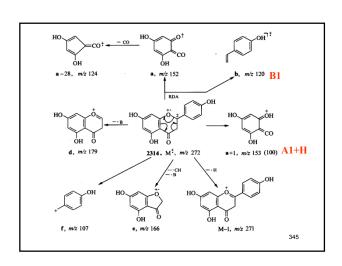
Nitrogen Rule

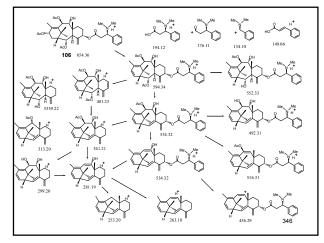
Nitrogen Rule: molecule with an odd number of nitrogens has an odd molecular weight; a molecule with only C, H, and O or with an even number of nitrogens has an even molecular weight.

342

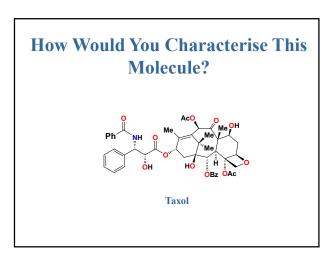


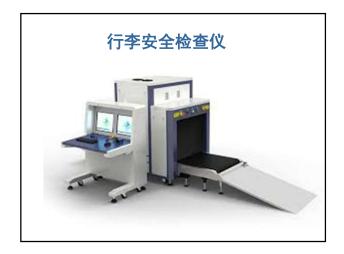


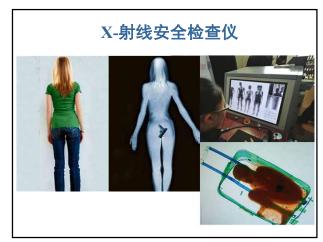


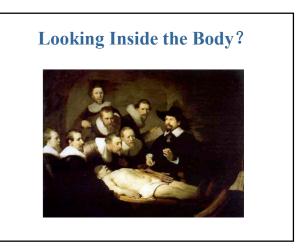




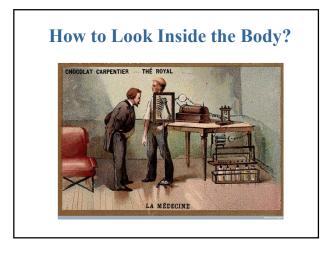


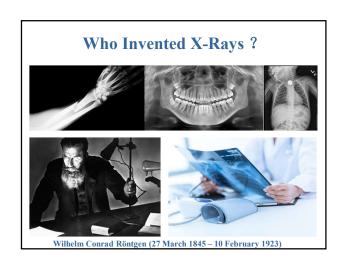












'I Have Seen My Death'

"Roentgen Rays"







Wilhelm Conrad Röntgen (1845 - 1923)

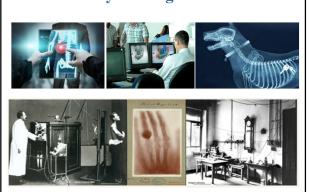
"My God, I see!"

The first X-rays by Wilhelm Röntgen, featuring the left hand of his wife Anna Bertha Ludwig on December 22, 1895. 《一种新射线——初步报告》 这是一张最著名的、后来在无数的教科书和博物馆里出现的那张照片

The International Day of Radiology-8th November Nov. 8, 1895: Roentgen Stumbles Upon X-Rays I did not think; Lexperimented. White Ronger Lexperimented and the location of the location o

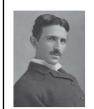
Wilhelm C. Röntgen 把X-射线的发明权无条件地献给了全人类

How X-Rays Changed the World?



Scenes from the Past

Nikola Tesla and the Discovery of X-rays







Nikola Tesla (1856–1943) fo One of mankind's most revered inventors

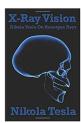
foot in a shoe. Tesla obtained in Mar.11, 1896 with X-rays

X-ray of a hand, taken by Tesla

The first X-rays by Wilhelm Röntgen was recorded On November 8, 1895

Nikola Tesla- The most important man of the 20th Century







Nikola Tesla (1856–1943)

Without his inventions and research, our modern world would look quite different-florescent lighting, x-ray machines, radio, television, cell phones, and more.

Trump and Rotational Radiation Therapy





John George Trump

Donald Trump And Nikola Tesla

Radiation therapy

On 7 January 1943 in New Yorker Hotel—and with fears being rampant that he had been working on a "Death Ray" to help the Allies win their war against the Nazis, the FBI immediately sealed off his room and called one of America's greatest scientific minds of that time to examine and catalog all of his work—whose name was John G. Trump, and who was the paternal uncle of 45th President Donald J. Trump.