HIGHLIGHTS FROM RECENT LITERATURE

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Each issue of *Gold Bulletin* contains key highlights from the research and patent literature. Authors who publish high-quality work in other journals are invited to send a copy of their publication to the editor for inclusion in the next issue.

Nanotechnology

Tuning the oriented deposition of gold nanorods on patterned substrates

The controlled patterning of anisotropic gold nanoparticles (NPs) is of crucial importance for many applications related to their optical properties. In this paper, Dutch researchers report that gold nanorods prepared by a seed-mediated synthesis protocol (without any further functionalization) can be selectively deposited on hydrophilic parts of hydrophobichydrophilic contrast patterned substrates (Ahmed et al., 2014 Nanotechnology 25(3):035301. doi:10.1088/0957-4484/25/3/ 035301). It is described that, when nanorods with lengths much smaller than the width of the hydrophilic stripe are used, they disperse on these stripes with random orientation and tunable uniform particle separation. However, for nanorods having lengths comparable to the width of the hydrophilic stripes, confinement-induced alignment occurs. Different interactions governing the assembly forces can be modulated by controlling the concentration of assembling nanorods and the width of the hydrophilic stripes, leading to markedly different degrees of alignment. This strategy can be replicated for other anisotropic nanoparticles to produce well-controlled patterning of these nanoentities on surfaces.

Shedding light on the growth of gold nanoshells

Nanostructured particles containing noble metals can have highly tunable localized surface plasmon resonances and are therefore of particular interest for numerous applications. Nanoshells comprising a dielectric core and gold or silver shell are a widely researched system because of the strong dependence of their optical properties on the ratio of core diameter to shell thickness. Although seededgrowth procedures have been developed to produce these particles, the many reported studies show significant variation in the nanoshell morphologies and hence optical properties. In order to establish processes that reproducibly synthesize nanoshells with high optical quality, it is necessary to develop techniques that monitor changes at the core particle surface during shell growth. For that purpose, researchers from the University of Erlangen-Nuremberg in Germany have carried out in situ nonlinear secondharmonic scattering (SHS) and linear vis-NIR extinction spectroscopy simultaneously during the seeded growth of gold nanoshells on silica core particles (Sauerbeck et al. ACS Nano, Article ASAP, doi: 10.1021/nn500729r). The SHS measurements show a striking variation in the nonlinear optical properties of the growing gold nanoshells. In comparison with linear optical measurements and with scanning electron microscopy (SEM) images made of gold nanoshells produced with varying shell completenesses, the SHS signal was observed to reach a peak intensity at a stage prior to shell closure. This is attributed to the high sensitivity of the SHS signal to the incomplete nanoshell surface morphology to the generation and subsequent degeneration of regions of electric field enhancement at gaps between isolated gold islands, which grow and coalesce. This conclusion is corroborated by finite-difference time-domain simulations of incomplete nanoshells. It is suggested that the in situ analytical approach demonstrated here offers significant promise for future activities regarding the in-process optimization of the morphology and optical properties of metal nanoshells and other nanostructured plasmonic particles.



Highly conductive ribbons prepared by stick—slip assembly of organosoluble gold nanoparticles

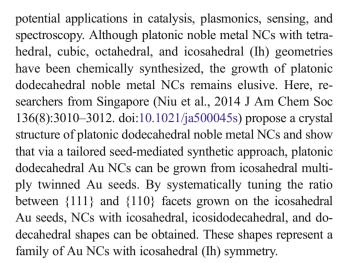
Precisely positioning and assembling nanoparticles (NPs) into hierarchical nanostructures is opening opportunities in a wide variety of applications. Many techniques employed to produce hierarchical micrometer and nanoscale structures are limited by complex fabrication of templates and difficulties with scalability. Here, a USA-based team describe the fabrication and characterization of conductive nanoparticle ribbons prepared from surfactant-free organosoluble gold nanoparticles (Au NPs) (Lawrence et al., 2014, ACS Nano 8(2):1173. doi:10.1021/ nn4057726). They used a flow-coating technique in a controlled, stick-slip assembly to regulate the deposition of Au NPs into densely packed, multilayered structures. This afforded centimeter-scale long, high-resolution Au NP ribbons with precise periodic spacing in a rapid manner, up to tow ordersof-magnitude finer and faster than previously reported methods. These Au NP ribbons exhibit linear ohmic response, with conductivity that varies by changing the binding headgroup of the ligands. Controlling NP percolation during sintering (e.g., by adding polymer to retard rapid NP coalescence) enables the formation of highly conductive ribbons, similar to thermally sintered conductive adhesives. Hierarchical, conductive Au NP ribbons represent a promising platform to enable opportunities in sensing, optoelectronics, and electromechanical devices.

Controlled assembly of peptide-functionalized gold nanoparticles for label-free detection of blood coagulation factor XIII activity

A highly sensitive label-free assay for the determination of blood coagulation factor XIII activity is demonstrated through the controlled assembly of peptide-functionalized gold nanoparticles (AuNPs) by a team from Imperial College London (Chandrawati, Stevens 2014 Chem Commun. doi:10.1039/ C4CC00572D). Factor XIII catalyzes the formation of covalent crosslinking between peptide chains through ε -(γ glutamyl)-lysine bonds leading to the aggregation of the AuNPs and consequently a red-shift of the localized surface plasmon resonance. The selective engineering of nanoscale order over AuNP crosslinking via the formation of isopeptide bonds provides a new approach toward the design of nanoassemblies with precise control on the molecular level. The colorimetric assay reported here provides direct qualitative and quantitative analysis of factor XIII activity with a limit of detection of 0.01 U mL⁻¹.

Dodecahedral gold nanocrystals: the missing platonic shape

Platonic noble metal nanocrystals (NCs) have attracted considerate attention due to their symmetry, aesthetic beauty, and



Gold nanoparticle-based tuberculosis immunochromatographic assay: the quantitative ESE Quanti analysis of the intensity of test and control lines

A rapid dual channel lateral flow assay for the detection of Mycobacterium tuberculosis antibodies (MTB 38 kDa monoclonal antibody) in human blood was developed by researchers at MINTEK in South Africa (Mdluli et al., Biosensors and Bioelectronics, Volume 54, 15 April 2014, Pages 1-6). The MTB 6–14–38 kDa fusion antigen and anti-Protein A were used as the capture proteins for test and control lines, respectively. Protein A labeled 40 nm gold nanoparticles were used as the detection conjugate. Whole blood and serum were spiked with MTB 38 kDa monoclonal antibody to make a positive sample model. The developed lateral flow was used to test MTB 38 kDa monoclonal antibody, and a detection limit of 5 ng/ml was used as a cutoff concentration of the analytes. The effect of the analyte concentration on the MTB lateral flow assay was studied using the variation of the intensity obtained from a ESE Quanti reader. There was a direct correlation between the analyte (MTB 38 kDa monoclonal antibody) concentration and the intensity of the test line. The intensity increased with an increase in the concentration of MTB 38 kDa monoclonal antibody, while in contrast, an increase in analyte concentration decreased the intensity of the control line.

Electronics

Connector with gold-palladium-plated contacts

Engineers at Apple Inc., describe an improved outer layer of plating comprising a binary metal alloy of gold and palladium on connector contacts (US2014045352 (A1)). The binary metal alloy is plated on at least the contact surface of the contacts. Intermediate plating layers can be



applied between the outer layer of gold and palladium and the conductive base of the contacts. The binary metal alloy of gold and palladium may be configured to have a mostly gold or a mostly silver appearance, depending upon the relative concentration of gold and palladium in the binary metal alloy.

Effects of bonding wires and epoxy molding compound on gold and copper ball bonds intermetallic growth kinetics in electronic packaging

This paper written by Malaysian researchers discusses the influence of bonding wires and epoxy mold compounds (EMC) on intermetallic compound (IMC) diffusion kinetics and apparent activation energies (Eaa) of CuAl and AuAl IMCs in a fineline ball grid array package (Gan et al., 2013, J Electron Mater. doi:10.1007/s11664-014-3011-y). The objective of this study is to study the CuAl and AuAl IMC growth rates with different epoxy mold compounds and to determine the apparent activation energies of different combination of package bills of materials. IMC thickness measurement has been carried out to estimate the coefficient of diffusion (Do) and Eaa various aging conditions of different EMCs and bonding wires. Apparent activation energies (Eaa) of both wire types were investigated after high-temperature storage life (HTSL) tests for both molding compounds. Au bonds were identified to have faster IMC formation, compared to slower IMC growth of Cu. The Eaa obtained for CuAl IMC diffusion kinetics are 1.08 and 1.04 eV with EMC A and EMC B, respectively. For AuAl IMC diffusion kinetics, the Eaa obtained are 1.04 and 0.98 eV, respectively, on EMCA and EMCB. These values are close to the previous HTSL studies conducted on Au and Cu ball bonds and are in agreement to the theory of HTSL performance of Au and Cu bonding wires. Overall, EMC B shows slightly lower apparent activation energy (Eaa) value as in CuAl and AuAl IMCs. This proves that the different types of epoxy mold compounds have some influence on IMC growth rates.

Gold bonding in semiconductor devices using porous gold

A patent from Alcatel-Lucent (US2014061921 (A1)) describes a method of manufacturing comprising providing a semiconductor layer having metal adhesion layer on a planar surface of the semiconductor layer and an alloy layer on the metal adhesion layer, the alloy layer comprising an alloy of gold and a non-gold metal. The method comprises removing a portion of the non-gold metal from the alloy layer to form a porous gold layer. The method comprises applying pressure between the porous gold layer and a metal layer to form a bond between the semiconductor layer and the metal layer.

Catalysis

Duel gold catalysis

For more than a decade, the innovative field of homogeneous catalysis by gold was dominated by the interaction of the substrate molecule with one gold center, in most cases in mononuclear gold complexes. The initial interaction was typically a π -coordination of a carbon–carbon double bond to the gold, an activation of the unsaturated substrate molecule by a π -acidic metal center. Only recently, clear evidence for reactions that involve the activation of organic substrates by two gold centers was obtained. In that new class of gold-catalyzed reactions, the two gold centers interact with the substrate in a very different way. One gold complex is σ -bonded to a terminal alkynyl group in the substrate; the other one is π coordinated. Only in a few cases, a combination π coordination and σ-coordination to the same alkyne, which is the energetically preferred mode of interaction with two gold centers, initiates the reaction. In most of the cases, the reaction proceeds through an intermediate with one alkyne σ bonded to one gold complex and a different alkyne π coordinated to the second gold complex.

Experimental and computational results for many new reactions provide a clear picture of the overall sequence of elemental steps of these conversions; some of the steps are unprecedented in organometallic catalysis and chemistry. For example, the reaction of divnes can involve gold vinylidenelike species as very reactive substructures formed by a 5-exodig cyclization. NBO analysis indicates no gold-carbon double bond character in these "vinylidenes." In other reactions, a 6-endo-dig cyclization is energetically preferred; after that, gold aryne complexes are not local minima but transition states of a 1,2-shift of gold. Computational studies showed a good correlation of the cyclization mode with the aromaticity of the intermediate. For both the 5-exo-dig and the 6-endo-dig cyclization modes, the intermediates are able to react even with unactivated alkyl C-H bonds, in low yields even in intermolecular reactions. The final step of the catalytic cycles is also remarkable, because the protodeauration has to occur with the next alkyne substrate molecule. Only then the next gold acetylide is formed directly and a loss of selectivity can be avoided. A computational study suggests that two gold complexes are on the substrate throughout the catalytic cycle. The most recent results indicate that analogous intermediates can be accessible by the reaction of other electrophiles with gold acetylides.

With regard to organic synthesis, the overall catalytic conversions open up a universe of new possibilities as described in this review by Stephen Hashmi (Stephen A. and Hashmi K. Acc. Chem. Res., Article ASAP, doi:10.1021/ar500015k). Selective C-H activations now allow to one use usually innocent alkyl side chains for



additional anellation reactions by an sp3-C–H activation. The C–H activation can even be combined with halogen transfer reactions, directly providing vinyl iodides as versatile building blocks. Short and efficient routes to different carbo- and heterocycles including benzocyclobutenes, fulvenes, and pentalenes demonstrate the synthetic potential not only for total synthesis but also for material science.

The direct synthesis of hydrogen peroxide using platinum-promoted gold–palladium catalysts

The direct synthesis of hydrogen peroxide offers a potentially green route to the production of this important commodity chemical. Early studies showed that Pd is a suitable catalyst, but recent work indicated that the addition of Au enhances the activity and selectivity significantly. The addition of a third metal using impregnation as a facile preparation method was thus investigated. The addition of a small amount of Pt to a CeO2-supported AuPd (weight ratio of 1:1) catalyst significantly enhanced the activity in the direct synthesis of H2 O2 and decreased the nondesired over-hydrogenation and decomposition reactions. The addition of Pt to the AuPd nanoparticles influenced the surface composition, thus leading to the marked effects that were observed on the catalytic formation of hydrogen peroxide. In addition, an experimental approach that can help to identify the optimal nominal ternary alloy compositions for this reaction is demonstrated in this publication from the Hutchings' lab (Edwards et al., 2014, Angew Chem Int Ed Engl 53(9):2384. doi:10.1002/anie.201308067).

A review on catalytic applications of Au/TiO2 nanoparticles in the removal of water pollutant

Nanomaterials are showing great potential for the improvement of water treatment technologies. In recent years, catalysis and photocatalysis processes using gold nanoparticles (Au-NPs) have received great attention due to their effectiveness in degrading and mineralizing organic compounds. This paper, written by Finnish and Iranian researchers, reviews and summarizes the recently published works and R and D progress in the field of photocatalytic oxidation of various water pollutants such as toxic organic compounds (i.e. azo dyes and phenols) by Au-NPs/TiO₂ under solar, visible and UV irradiation (Ayaki et al., 2014, Chemosphere. doi:10.1016/j.chemosphere.2014. 01.040). Extensive research which has focused on the enhancement of photocatalysis by modification of TiO₂ employing Au-NPs is also reviewed. Moreover, the effects of various operating parameters on the photocatalytic activity of these catalysts, such as size and loading amount of Au-NPs, pH and calcination, are discussed. The support type, loading amount and particle size of deposited Au-NPs are the most important parameters for Au/TiO_2 catalytic activity. This study highlights that the modification of TiO_2 , including semiconductor coupling, can increase the photoactivity of Au/TiO_2 . In contrast, doping large gold NPs can mask or block the TiO_2 active sites, reducing photocatalytic activity. The optimized loading amount of Au-NP varied for each experimental condition. Finally, research trends and prospects for the future are briefly discussed.

New insights into the catalytic activity of gold nanoparticles for CO oxidation in electrochemical media

This study by British and Dutch research groups reports the interaction between metal oxides and gold in acidic media and its effect on the electrochemical oxidation of carbon monoxide (Rodriguez et al., Journal of Catalysis, Volume 311, March 2014, Pages 182–189). They describe the oxidation of CO in acidic media on Au nanoparticles of 3 and 7 nm on different oxide supports, diamond and carbon electrodes. In addition, the effect of a ${\rm TiO}_{\rm x}$ support on Au nanoparticles was mimicked by supporting ${\rm TiO}_{\rm x}$ nanoparticles on bulk gold. The comparison of these two systems strongly suggests that electronic interactions between Au and ${\rm TiO}_{\rm x}$, rather than Au nanoparticle size effects, are the driving force of the catalytic activity in ${\rm Au-TiO}_{\rm x}$.

Catalysis on nanoporous gold–silver systems: synergistic effects toward oxidation reactions and influence of the surface composition

Au-Ag nanoporous systems were prepared by a method recently developed by French researchers (Déronzier et al., Journal of Catalysis, Volume 311, March 2014, Pages 221-229). Contrary to the electrochemical dealloying, the methodology applied in this work proved that it allowed to prepare bimetallic AuAg NP systems with controlled chemical compositions. Compared with monometallic Au or Ag catalysts, the alloy catalysts exhibited high activity toward CO and/or H₂ oxidation and exceptionally high selectivity at low temperature for CO oxidation in the presence of H2 showing a synergistic effect between Au and Ag. Among the different characterizations, low-energy ion-scattering experiments provided composition data about the topmost atomic layer, i.e., where catalytic reactions occur and allowed us to establish a clear correlation between top layer surface concentration and reactivity. A pronounced dependence of the reaction rate on the silver concentration has been observed only for H₂ oxidation. This strong dependence has been correlated with the number of surface sites constituted of adjacent Ag atoms required for dissociative oxygen adsorption. The high selectivity of the Au-Ag alloys with respect to pure gold has been ascribed to a large segregation of silver, especially on low coordination sites, inhibiting the H₂ adsorption.



Selective oxidation using supported gold bimetallic and trimetallic nanoparticles

Supported gold nanoparticles are highly effective for a range of redox reactions. In these reactions, the activity is often enhanced by the addition of a second or indeed a third metallic component. A model reaction that is often investigated is the selective oxidation of benzyl alcohol using molecular oxygen as terminal oxidant. In the presence of a solvent, the complexity of this reaction can often be missed. However, in the solvent-free oxidation of benzyl alcohol to benzaldehyde using supported gold palladium nanoparticles as catalysts, there are two pathways to the principal product, benzaldehyde. One is the direct catalytic oxidation of benzyl alcohol to benzaldehyde by O2, while the second is the disproportionation of two molecules of benzyl alcohol to give equal amounts of benzaldehyde and toluene. The formation of toluene is an unwanted side reaction. In this paper, Graham Hutchings reviews research on this reaction and two strategies described that can be used to switch off the formation of the nondesired toluene (Hutchings Catalysis Today. doi:10.1016/ j.cattod.2014.01.033). The first involves the use of basic supports for the gold palladium nanoparticles, which is highly effective in suppressing the formation of toluene, and this may be related to the morphology of the gold palladium nanoparticles and their interaction with the support. The second involves the introduction of platinum to the gold palladium nanoparticles which also switches off toluene formation on supports that permit toluene formation in the absence of platinum. This effect may be related to the relative stability of platinum hydride.

Chemistry

Monodentate gold ethynyl complexes

GE scientists describe monodentate gold ethynyl complexes having a gold–carbon bond and a gold–phosphorous bond, which may be useful in optoelectric devices. The complex constituents are independently monocyclic or polycyclic aryl, unsubstituted or substituted with one or more alkyl, alkenyl, alkoxy, aryl, aryloxy, fluoro, fluoroalkyi, or perfluoroalkyl, and a substituted or unsubstituted aryl (WO2014021997 (A1)).

Fischer-type gold(I) carbene complexes stabilized by aurophilic interactions

(Bezuidenhout et al., 2014, Dalton Trans 43:398–401, 10. 1039/C3DT52961D) describe the synthesis and structure of rare acyclic alkoxy- and aminocarbene complexes of gold(I), including a novel ferrocenophane dinuclear biscarbene

complex. X-Ray diffraction analyses and DFT calculations reveal that these complexes are stabilized by genuine aurophilic interactions.

Reversible thermal-mode control of luminescence from liquid-crystalline gold(I) complexes

The synthesis and characterisation of liquid-crystalline (LC) gold complexes designed to have a rod-like structure in dimeric form is described by Japanese researchers (Jujisawa et al., 2014, J Mater Chem C. doi:10.1039/C3TC31973C), and the relationship between their photophysical properties and aggregated structure discussed. The luminescence intensities of the complexes were enhanced in the condensed phase, meaning that the complexes showed aggregationinduced emission. Observed photoluminescence in the condensed phase could be assigned to a monomer emission; however, luminescent properties were strongly affected by the aggregated structures of the complexes. A reversible "on-off" switching of the luminescence induced by the phase transition between LC and isotropic phases was demonstrated. Moreover, complex 1b showed thermochromic photoluminescence controlled by the aggregated structure; the color of luminescence could be reversibly controlled by the phase transition between crystalline and LC phases. These LC gold complexes show potential application as materials for novel light-emitting devices.

Medicine

Gold nanoparticles for nucleic acid delivery

Gold nanoparticles provide an attractive and applicable scaffold for delivery of nucleic acids. In this review, a team led by Vince Rotello at Amhurst focus on the use of covalent and noncovalent gold nanoparticle conjugates for applications in gene delivery and interfering RNA technologies (Ding et al., 2014, Mol Ther. doi:10.1038/mt.2014.30). Also discussed are the challenges involved in nucleic acid delivery, including endosomal entrapment/escape and active delivery/presentation of nucleic acids in the cell.

Gold nanoparticles in breast cancer treatment: promise and potential pitfalls

Despite remarkable achievements in the treatment of breast cancer, some obstacles still remain. Gold nanoparticles may prove valuable in addressing these problems owing to their unique characteristics, including their enhanced permeability and retention in tumor tissue, their light absorbance and surface plasmon resonance in near-infrared light, their interaction with radiation to generate secondary electrons, and their



ability to be conjugated with drugs or other agents. Herein, MD Anderson scientists and medics discuss some basic concepts of gold nanoparticles and early results from studies regarding their use in breast cancer, including toxicity and side effects. Also discussed are these particles' potential clinical applications (Lee et al., 2014, Cancer Lett. doi:10. 1016/j.canlet.2014.02.006).

Site-specific targeting of enterovirus capsid by functionalized monodisperse gold nanoclusters

Development of precise protocols for accurate site-specific conjugation of monodisperse inorganic nanoparticles to biological material is one of the challenges in contemporary bionanoscience and nanomedicine. Finnish researchers report a successful site-specific covalent conjugation of functionalized atomically monodisperse gold clusters with 1.5-nm metal cores to viral surfaces (Marjomäki et al., 2014, Proc Natl Acad Sci U S A 111(4):1277-1281. doi:10. 1073/pnas.1310973111). Water-soluble Au102(paramercaptobenzoic acid)44 clusters, functionalized by maleimide linkers to target cysteines of viral capsid proteins, were synthesized and conjugated to enteroviruses echovirus 1 and coxsackievirus B3. Quantitative analysis of transmission electron microscopy images and the known virus structures showed high affinity and mutual ordering of the bound gold clusters on the viral surface and a clear correlation between the clusters and the targeted cysteine sites close to the viral surface. Infectivity of the viruses was not compromised by loading of several tens of gold clusters per virus. These advances allow for future investigations of the structure-function relations of enteroviruses and enterovirus-related virus-like particles, including their entry mechanisms into cells and uncoating in cellular endosomes.

Auranofin is an apoptosis-simulating agent with in vitro and in vivo anti-leishmanial activity

Cutaneous leishmaniasis remains ignored in therapeutic drug discovery programs worldwide. This is mainly because cutaneous leishmaniasis is frequently a disease of impoverished populations in countries where funds are limited for research and patient care. However, the health burden of individuals in endemic areas mandates readily available, effective, and safe treatments. Of the existing cutaneous leishmaniasis therapeutics, many are growth inhibitory to *Leishmania* parasites, potentially creating dormant parasite reservoirs that can be activated when host immunity is compromised, enabling the reemergence of cutaneous leishmaniasis lesions or worse spread of

Leishmania parasites to other body sites. To accelerate the identification and development of novel cutaneous leishmaniasis therapeutics, the University of Virginia researchers designed an integrated in vitro and in vivo screening platform that incorporated multiple Leishmania life cycles and species and probed a focused library of pharmaceutically active compounds (Sharlow et al., 2013, ACS Chem Biol. doi:10.1021/cb400800q). The objective of this phenotypic drug discovery platform was the identification and prioritization of bona fide cytotoxic chemotypes toward Leishmania parasites. The Food and Drug Administrationapproved drug auranofin, a known inhibitor of Leishmania promastigote growth, was identified as a potent cytotoxic anti-leishmanial agent and inducer of apoptotic-like death in promastigotes. Significantly, the anti-leishmanial activity of auranofin transferred to cell-based amastigote assays as well as in vivo murine models. With appropriate future investigation, these data may provide the foundation for potential exploitation of gold(I)-based complexes as chemical tools or the basis of therapeutics for leishmaniasis. Thus, auranofin may represent a prototype drug that can be used to identify signaling pathways within the parasite and host cell critical for parasite growth and survival.

Multifunctional theranostic gold nanoparticles for targeted CT imaging and photothermal therapy

Gold nanoparticles have emerged as some of the most extensively utilized nanoplatforms for the diagnosis, imaging, monitoring, and treatment of malignant diseases. In particular, in computed tomography (CT) imaging and in therapy (PTT), the exploitation of the various, advantageous properties of gold nanoparticles have resulted in numerous advances in each of these fields. This review, authored by a team from the University of Michigan, assesses the status of gold nanoparticle-mediated CT and PTT, highlight several promising outcomes, and motivate the combination of these two functionalities in the same nanoparticle platform (Curry et al., 2014 Contrast Media Mol Imaging 9(1):53-61. doi:10.1002/cmmi.1563). The given examples of researchbased advances and the encouraging results of in vitro and in vivo studies provide much excitement and promise for future theranostic (therapy + diagnostic) clinical applications, as well as for image-guided therapy and/or surgery, and their monitoring.

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